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Just Ready!—Stokes, Beerman & Ingraham's Modern Clinical Syphilology

The New (3rd) Edition is just off press!—The New (3rd) Edition that literally hundreds and hundreds of doctors, in the Service, in civilian practice—family physicians, syphilologists, dermatologists and other specialists—have been so eagerly, so expectantly awaiting.

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AN ARSENICAL WITH A BRILLIANT RECORD OF EFFECTIVENESS AND SAFETY

MAPHARSEN

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A SUBACUTE GENERALIZED NEUROMUSCULAR EXHAUSTION SYNDROME

CHAIRMAN'S ADDRESS

J. M. NIELSEN, M.D.
LOS ANGELES

A syndrome of extreme weakness with muscular atrophy and fascicular twitching as the direct result of overwork forms the subject of this communication. In view of the extreme stresses to which men are subjected in war it seems impossible that the syndrome here described can be new in the literature, but no record of any case prior to the one reported in 1940 has been found.

Muscular atrophy with fascicular twitching occurs under many conditions. It is the most prominent sign of progressive spinal muscular atrophy, but, as Oppenheim [1] warned over thirty years ago, it is not pathognomonic of that disease. He stated that fibrillation could occur in normal persons "after excesses." Russell Brain [2] lists in addition to the progressive spinal muscular atrophies of adults and of children such entities as the Charcot-Tooth-Marie disease and progressive hypertrophic neuritis as conditions in which atrophy and fibrillation occur. In focal areas the syndrome is commonly seen as the result of irritation of the motor spinal roots by neoplasm or exostoses.

Brain and Turnbull [3] have given special attention to atrophy and fasciculation as symptoms of thyrotoxicosis. They consider the weakness of the muscles in exophthalmic ophthalmoplegia a result of the thyrotropic hormone of the anterior pituitary gland. McEachern and Ross [4] collected 10 cases of generalized muscular atrophy and fasciculation due to thyrotoxicosis and added a few of their own. In that condition the girdles are more involved than are the small muscles of the hands. By far the most striking fact about such cases, however, is that recovery follows thyroidectomy.

It is common knowledge that an arm may show extreme weakness and fascicular twitching as the result of overwork with such tools as compressed air drills or hammers in a person unaccustomed to such work. I do not refer to compression neuritis of the small nerves of the palm but to atrophy of the muscles of the forearm and even of the arm from strain and vibration. Maassen and Büttner [5] have observed muscular atrophy in the arm with small foci of degeneration in the cervical cord from work with a compressed air hammer. Whether the spinal cord changes are primary, secondary or coincidental is difficult to determine. The authors ascribe them to the vibration, which affects not only the arms but the entire spine and therefore the spinal cord.

In a thorough analysis of the subject of fibrillation and fasciculation, Denny-Brown and Pennybacker [6] have shown the anatomic differences between fibrillation and fasciculation. Using concurrent mechanical and electrical recording they verified an old observation that true fibrillation follows complete denervation and appears five days after nerve section in the human subject. They observed true fibrillation after poliomyelitis and polyneuritis and in a case of syringomyelia. Fibrillae are supplied by single nerve fibers and hence are "nerve units," while fasciculi are supplied by many fibers and are not units in the same sense but on the other hand they are supplied by a single vessel and are "vascular units." Fascicular twitchings may thus result from toxins circulating in the blood.

The same authors consider idiomuscular contractions probably the result of stimulation of the sarcoplasm rather than of the sarcolemma (which receives the nerve impulse). In circumstances of fatigue or excessive loss of sodium chloride involuntary muscular contractions appear. "Those due to fatigue are small bursts of contraction in a fasciculus and are of a type such as would be caused by irregular discharge spreading to and through all the nerve bundles in the fasciculus." The involuntary contractions of myokymia associated with hyperhidrosis are of a similar nature.

The cases which form the clinical material of the present paper are instances of widespread muscular atrophy with fascicular twitching resulting from exhaustion. Clinical examination of a patient at the height of the disease, in the absence of history, would lead the examiner to suspect progressive spinal muscular atrophy. But with an adequate history one can soon determine that an entirely different syndrome is at hand. The onset is sudden, the recovery slow and usually incomplete but the prognosis as to life is good.

Four cases are included in this report. The first is quoted with minor editorial corrections from an article of mine [7] published in 1940. The second and third are new ones and the fourth is abstracted from a paper by Marsh.[8]

Read before the Section on Nervous and Mental Diseases at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 14, 1944.

1. Oppenheim, H.: Lehrbuch der Nervenkrankheiten, Berlin, S. Karger, 1913, p. 307.
2. Brain, W. R.: Diseases of the Nervous System, London, Oxford University Press, 1933.
3. Brain, W. R., and Turnbull, H. M.: Exophthalmic Ophthalmoplegia, Quart. J. Med. **7**: 293, 1938.
4. McEachern, D., and Ross, W. D.: Chronic Thyrotoxic Myopathy, Brain **65**: 181, 1942.
5. Maassen, R., and Büttner, H. E.: Halsmarkdegeneration mit sekundärer Muskelatrophie durch Arbeit am Presslufthammer, Arch. f. Gewerbepath. u. Gewerbehyg. **10**: 19 (April) 1940.
6. Denny-Brown, D., and Pennybacker, J. B.: Fibrillation and Fasciculation in Voluntary Muscle, Brain **61**: 311, 1938.
7. Nielsen, J. M.: Subacute Generalized Neuromuscular Exhaustion Syndrome, Bull. Los Angeles Neurol. Soc. **5**: 128 (June) 1940.
8. Marsh, C.: Subacute Generalized Neuromuscular Exhaustion Syndrome, Bull. Los Angeles Neurol. Soc. **8**: 65 (June) 1943.

REPORT OF CASES

CASE 1.—*Severe overexertion followed by extreme muscular asthenia and atony, loss of body weight and generalized tenderness. Only partial recovery in a year.*

G. D. H., a blond business executive aged 42, was referred by Dr. G. H. Beck of Glendale, Calif., because of severe asthenia still persisting seven weeks after acute overexertion. The patient was an only child of healthy parents still living and well. In the personal history there was record of measles, mumps, pertussis, chickenpox, tonsillitis and one accident at the age of 23 years in which he sustained fracture of an ankle.

The patient was an almost complete extrovert. He held a political position but had a reputation for highly efficient management and great accomplishment. His spare time was devoted entirely to lodge organization and he held not only local but district offices, so that his evenings were taken almost exclusively with meetings, which he usually addressed with stimulating talks. He was considered not only by himself but by his associates as indefatigable; he usually retired some time between midnight and 2 a. m. To all this his wife did not object; she regarded it as her job to be collaborator in helping her husband "reach the top," and consequently there was no associated emotional strain.

His policy was to take part in every phase of social life, to drink a little when necessary, never to excess, and to eat at odd hours with casual acquaintances, all of which gave him a very irregular life so far as rest and nutrition were concerned. He obtained from five to seven hours of sleep a night, never having required more to feel rested in the morning.

He considered himself entirely well up to Sept. 4, 1938, when he attended a lodge picnic. He acted as catcher for his baseball team, organized at the site, through the first five innings. He remarked "And when I say I played, I mean I played." He seemed to have unbounded energy until the end of his period as catcher, but in the sixth inning he could hardly support himself in a squatting position and, "for a change," he took the job of pitching through the sixth and seventh innings. By that time he simply could not stand and was forced to admit physical defeat. He sat down for nearly an hour too exhausted to take a bath. He then changed clothes, drove home, took a hot and cold shower (enervating after exhaustion) and fell into a sleep.

Awakened by his wife, he ate a little supper and retired for the night. But he could not sleep; instead he rolled and tossed incessantly. In the morning he arose at 6 expecting to be sore and stiff all over. To his surprise he was not stiff at all; but he was "practically paralyzed." His muscles were exquisitely tender, so that it was painful to lie or sit. Still he did not consider the condition serious and went to his office, where he found it possible to sit in his chair and write.

The second night was as bad as the first, and the second day found him "sore in every joint in the body." The pain increased, and during the third night he slept only three hours. On the third day he was unable to tie his shoelaces and could not hold up his arms long enough to tie his necktie. After his wife had dressed him he could not cross one knee over the other. On a scheduled business trip he found it impossible for the first time in his life to drive his car but went with a driver and drove part of the way.

On his return his nights continued very bad. When he could not sleep he got up and paced the floor in a frenzied restlessness. He then consulted Dr. Beck, who gave him salicylates for his pain and vitamin B_1 and ordered continued rest. He obtained considerable relief from pain but immediately tried to do more work. He lost 15 pounds (6.8 Kg.) in spite of a good appetite and in the seventh week developed a series of "fever blisters" on his buttocks. These disappeared spontaneously.

When I examined him on October 26 he appeared pale and thin. His entire demeanor was that of a person utterly exhausted. He spoke slowly and without force. He sank into a chair as though hardly able to stand. His body weight was 147 pounds (67 Kg.; normal for him 165 pounds, or 75 Kg.), his blood pressure was 112 systolic and 80 diastolic, the pulse rate 80 per minute. His arteries were palpable but not sclerosed. The heart, lungs and abdominal viscera were normal. The temperature was 98 F.

His musculature was as flabby as that seen in acute anterior poliomyelitis during the stage of paralysis, but the atony was generalized. The muscles were too tender to make determination of nerve trunk tenderness definite. Fibrillary and coarse fascicular twitchings were noted only in the right serratus anterior muscle. The infraspinatus muscles were concave instead of convex, but no specific atrophy could be discovered. In spite of all this the deep and superficial reflexes were entirely normal. Pathologic reflexes were not found. There were no sensory changes.

In order to get for the patient the rest so urgently required, I told him forcefully that he would go on to paralysis and death if he did not obtain ten hours of sleep each night by the use of sedatives if necessary. Vitamins were recommended in large doses, and the patient was referred back to his family physician. Dr. Beck carried out the treatment.

The patient was referred for another examination Dec. 15, 1938. He had gained 6½ pounds (3 Kg.), the tone had returned in his muscles, he talked with more energy, and he was able to stand for a few minutes without undue fatigue. He was sleeping well and the muscular soreness had disappeared, but there was definite tenderness of the nerve trunks. His grip had improved from 28 to 35 on the right and from 18 to 30 on the left.

A new complaint had developed, muscular spasms in the calves, thighs and arms which the patient and his wife "massaged out." He was, however, able to rise from a squatting posture without use of his arms, but in walking over irregularities he stumbled and fell, especially over pebbles and irregularities in carpets. His recovery seemed to be only a matter of time. Report one year later showed that he had far less endurance than he had before the episode described.

This case seems to present a severe exhaustion of the striped neuromuscular apparatus, with a condition of the muscles which might be termed myositis except that it was not inflammatory. The nerves also were affected but not in a way to prevent conduction of impulses. The residual tenderness of the nerve trunks shows that the process was neural as well as muscular, and the localized muscular spasms point in the same direction. It is for these reasons that I call the condition a subacute generalized neuromuscular exhaustion syndrome.

CASE 2.—*Excessive physical exertion followed by gradual paralysis of all four limbs and diaphragm. Evidence of central involvement of the cervical cord but extreme atrophy of both shoulder and pelvic girdles.*

Roy K., a white man aged 37, who normally weighed about 149 pounds (67.6 Kg.), always a physical rather than an intellectual worker, considered himself well up to the last week of May 1943. His history of past illnesses included the usual childhood diseases but not any of the severe illnesses, and he had had no surgical operations.

His habits are of prime importance in the illness to be discussed. He was born in Minnesota on a farm and was accustomed to farm labor. His education had been meager, but his handicap was overcome by an unusual industriousness. He had a wife and two children, 10 and 14 years of age respectively, for whom he was gradually buying a home. His type of work varied somewhat with the season of the year. For some months prior to his present illness he had held two jobs. One of these consisted in driving a school bus, gathering the children from a large area before school hours and redistributing them afterward. His accessory duties extended the time of this employment to six hours daily. His other job was that of warehouse worker, particularly that of stacking bags of sugar weighing 100 pounds (45 Kg.) each. He was proud of the fact that,

though of moderate build, he could stack 1,000 bags in eight hours. He thus picked up and stacked, by means of a lift and a thrust of his body, 100,000 pounds (45,450 Kg.), or 50 tons, a day. It is of importance to note that in this work the pelvic and shoulder girdles and the spine were utilized much more than the smaller muscles of the extremities.

During the working day of May 27, as a large consignment of sugar had been stacked, his foreman announced that they would now go to another warehouse to stack another load. For the first time in his life the patient announced that he would have to go home to rest. He felt too weak to continue and pointed out that he had been obtaining only four and a half to five and a half hours of sleep a night for a long time. He was allowed to go to his home.

On arriving at his home he lay down to rest but found that he was restless and was more inclined to keep moving. He was extremely tired and "sore," and his arms particularly were painful but he could not relax. There were generalized painful muscle "cramps." He took a mild barbiturate and went to sleep. When he awoke the following morning he was not any better; he thought he was even more tired. He could barely walk about. He therefore remained at home for another twenty-four hours and spent his time taking sun baths. There were fewer muscle spasms. On the morning of the third day he was paralyzed in all four limbs.

The first physician called took some tests but could not make a diagnosis. For that reason the family called a cultist, who gave strict dietary instructions and limited the patient's intake "to 485 calories a day." As the patient became weaker and had difficulty with breathing, a second physician was called, who had more laboratory work done and had the patient hospitalized. This work was done from June 11 to July 2 and the results were as follows:

Blood counts: Red cells 4.2, 3.8, 4.4, 3.6 and 3.3 millions per cubic millimeter; hemoglobin content 10.2 to 12.5 Gm. per hundred cubic centimeters of blood; white cells 7,200, 5,800, 5,100, 6,600 and 9,300 per cubic millimeter; total neutrophils 64 per cent to 76 per cent; segmented cells constituted 57 per cent, later 44 per cent.

The nonprotein nitrogen was 31.5, sugar 86 and calcium 8.6 mg. per hundred cubic centimeters of blood. The blood culture was sterile. The agglutination test for Brucella abortus and the Wassermann reaction were both negative. Blood culture was sterile, and a sputum examination was negative. The spinal fluid was clear and contained 3 cells per cubic millimeter. The globulin was negative and the sugar content was reported as normal. It was negative for bacteria.

Two urine specimens had a specific gravity of 1.007 and 1.028. The p_H was 4 and 4.5. There were no abnormal constituents in either specimen, but creatine was not tested for.

The patient had already been treated with all sorts of vitamins in large quantities and was on an excellent diet. His appetite was good.

I saw the patient for the first time on July 12, about six weeks after the onset of the acute illness and observed a striking physical condition. The patient was 5 feet 10 inches (178 cm.) tall but in a poor state of nutrition. The shoulder and pelvic girdles were almost without musculature. The supraspinati were nearly absent, the deltoids very small, the infraspinati better preserved. The arms were small, the forearms and hands essentially normal. The patient could not raise either upper limb from the bed but could manipulate his fingers to crawl up the clothes to his face. The pelvic girdle was almost denuded of muscles, the condition resembling that of a long wasting disease. The buttocks were hollow and the anus was an opening on a flat surface. The thighs were somewhat atrophic, but the legs and feet were normal. He was able to flex and extend his lower limbs in bed when there was no weight on them. In harmony with this state the deep reflexes were all absent in the upper limbs, and the knee jerks were absent. The achilles reflexes were present. No pathologic reflexes were found anywhere. His weight was estimated at about 75 pounds (34 Kg.). The blood pressure was 126/86, the pulse rate 90 per minute. The heart and lungs were normal. The thyroid gland and lymph glands were not palpable.

Most striking was the patient's breathing during the taking of his history. He was extremely dyspneic, and with each inspiration the abdominal wall was retracted; there was almost complete paralysis of the diaphragm. Fibrillary twitchings were seen on the thorax. The umbilicus moved cephalad one-half inch when he attempted to raise his head off the pillow.

The cranial nerves were entirely normal except for hoarseness, which had developed with the onset of his illness. The tongue was not atrophic.

Sensory examination gave the examiner another surprise. Sensory perception was normal except for loss of pain and temperature perception from the third cervical to the fourth dorsal segments inclusive, the hands partly escaping.

I recommended treatment with a high caloric, high vitamin diet, 4,000 calories per day supplemented with injections of thiamine hydrochloride 50 mg. per day for six weeks. He was also to take wheat germ oil 1 drachm (4 cc.) three times daily and aminoacetic acid 1 ounce (30 Gm.) twice daily. As soon as his strength should permit he was to have exercises in a pool.

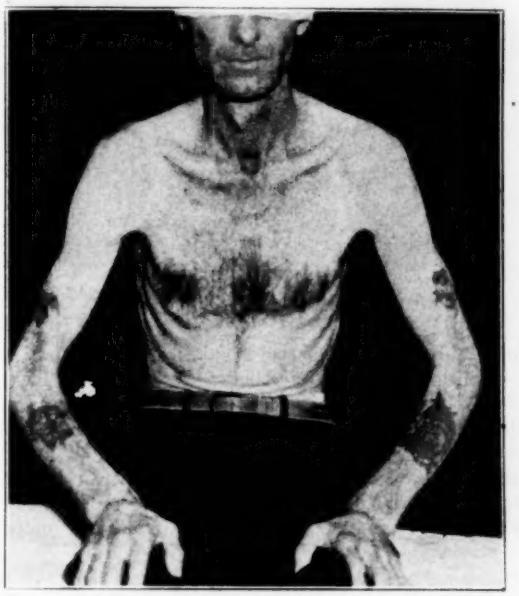

Fig. 1 (case 2).—Appearance of patient after he had gained 30 pounds (13.6 Kg.). Weight at time of photography, 105 pounds (47.6 Kg.).

The patient was not seen again until December 23, when he was referred by his new physician after the sudden death of his former one. This time he came to my office and I was able to obtain photographs and to do electrical tests on his muscles (figs. 1, 2 and 3).

The follow-up history was to the effect that he had made rapid improvement on the regimen advised. On July 14 he was removed to his home. By the first week of August he was able to feel pin prick again where its perception had been absent. By the middle of August he was able to walk around, and soon after that time he was able to raise his arms above his head. However, atrophy of the interossei had set in after my first visit. By the 1st of November he was able to drive his automobile. Next he resumed light duty on his ranch, feeding calves and looking after a pig. He ceased taking aminoacetic acid October 1, having decided that he did not need it any longer.

December 5 he drove his car 50 miles in one stretch, and when he reached his destination he felt weak. He ate a big meal and went to bed, but on the following day he had severe muscular pains which felt like cramps all over his body and he was unable to obtain any relief. For that reason he took a warm immersion bath, relaxed and fell asleep in the water, where

his wife found him later so soundly asleep that she could hardly arouse him. He was then too weak to be up, and from that time until December 23, when I saw him, he was in bed about half of the time.

Examination December 23 showed that he had had an exacerbation of his acute illness. He had lost 20 (9 Kg.) of the 50

Fig. 2.—Atrophy of shoulder girdle.

pounds (23 Kg.) which he had regained after the first episode (weight on examination 105 pounds, or 47.6 Kg.). There was pronounced atrophy of the shoulder girdle and of the arms (as shown in the illustrations). There was also some atrophy of the interosseus muscles but not of the thenar or hypothenar eminences. His buttocks were much better than at the time of my first examination, but they were still very small. His temperature was 97.8 F., blood pressure 138/80, pulse rate 90 per minute.

All deep reflexes were present and about normal. All superficial reflexes were present, and pathologic reflexes were not obtained. He was barely able to walk around, and standing for a few minutes fatigued him. His hoarseness had disappeared and his breathing was normal.

He was unable to extend the middle and ring fingers of the right hand completely. While no myotonia could be demonstrated, he was able to open and close his fists only slowly, and exercise of the hands brought on rapid weakness. There was no sensory loss anywhere.

The affected muscles were tested for reaction of degeneration. Faradic irritability was demonstrated in all muscle groups with the exception of the finger extensors in both forearms. Those muscles responded slightly to the galvanic current, better to the cathodal than to the anodal pole. There was therefore a partial reaction of degeneration.

On Jan. 3, 1944 his wife telephoned to say that the downward course was still in progress; the patient was at the time unable to open his hands, though he could make a weak fist.

On February 6 the patient's wife reported by mail. She was giving him all treatment recommended and he had a good appetite for the first time since the onset of his illness. After having lost completely the use of his hands early in January he had in four weeks regained ability to open and close his hands and to use "the thumb and first fingers fairly well." However, he had a wrist drop on both sides. He was gaining in weight as shown by the body in general "filling out nicely," but his arms remained atrophic.

On March 23 another communication was received to the effect that the patient had regained lost weight and weighed 135 pounds (61 Kg.). He was feeling well and had a good appetite. He was up and had resumed care of his garden, calves and chickens. He was again able to straighten his fingers, and the muscles of his hands were "filling out." He wanted to know whether he could stop his medicine and start driving his car.

It is evident that he cannot learn his limitations; when he gathers a little strength he immediately proceeds to expend it.

With this course of the illness besides the findings as a background I feel that there is little doubt that the entire syndrome was the result of neuromuscular exhaustion. As the area most severely affected—that supplied by the lower cervical cord—at the first instance showed loss of perception of pain and after many months still showed a partial reaction of degeneration in certain muscle groups, it seems clear that the exhaustion may leave permanent residuals due to cord changes. However, the pyramidal tract apparently did not suffer, as there were no pathologic reflexes and there was no increase in the deep ones. It is barely possible that the loss of perception of pain in the arms was hysterical in nature, especially since the hands partly escaped, and that the spinal cord involvement was confined to the lower motor neurons.

CASE 3.—*Long continued starvation simultaneously with excessive exercise prescribed by physical education teacher in school. Loss of weight from 145 to 115 pounds (66 to 52 Kg.) in three months. Gradual continuation of exercise and starvation for two years with complete asthenia.*

L. G., a white girl aged 17 years, was seen privately because of chronic exhaustion which had been diagnosed myasthenia gravis. Up to the age of 14 years she was a "fat girl" but became sensitive about her state of nutrition at that time.

Fig. 3.—Appearance of back and arms.

When she was 14 years of age and in the eighth grade in school an athletic director instituted Danish gymnastics for the classes. The patient took all of the prescribed work faithfully and at the same time decided to reduce her weight. She ate "practically nothing" for three months and reduced her weight from 145 to 115 pounds. Her sister added that before the reduc-

tion the patient was a glutton, eating "all of the time," but after the reduction in weight she had lost her appetite and could not eat when she had decided to resume her normal diet. She developed muscular twitchings in various parts of her body, which continued for a number of months, and her muscles shrank visibly. She became "terribly nervous" and was unable to remain quiet in the daytime but tended to sleep if she could ever relax. She continued the heavy Danish gymnastic exercises after her loss of weight.

In the fifteenth year of her life she began to gain a little in weight, but she watched her weight strictly and would again starve whenever she showed any gain. She continued her strenuous exercises and became so weak that she could hardly walk about.

She started her junior year (sixteenth year) but had to quit school and was taught by a home teacher. She was in bed most of the time, but at times when she had invitations to perform on the stage in gymnastics she could not refrain and thus used all of her strength for performances and went to bed afterward. At this stage her mother became aware that the girl was losing her health and had her see a doctor. The latter, however, said that there was nothing wrong with her. He considered the condition functional and stated that her psychology was bad. Her eyes were sensitive to light and she stayed indoors and wore dark glasses.

She then consulted doctors at a clinic and had many tests, all of which were said to be normal. An "old doctor" took over the case and after making another examination made a diagnosis of myasthenia gravis. He also considered thyroid trouble and treated her for one period of time for one thing, then for the other.

She made no progress on neostigmine methylsulfate. She was then treated with large doses of various vitamins. On thiamine hydrochloride she was said to become "wild." She then consulted a chiropractor, who made a diagnosis of Streptococcus viridans infection of the ovaries and treated her with adjustments. He also prescribed alfalfa and calcium.

When I saw her a history was obtained of tonsillectomy early in life and of a streptococcic sore throat. Her periods were regular but painful, and she complained of hot flashes. Her basal metabolic rate had been reported as "normal."

The patient was tall. She weighed 110 pounds (50 Kg.) and lay quietly in bed. She wore dark glasses, with all window shades drawn. She answered all questions relevantly but with an air of fatigue. The blood pressure, which had been reported as 90 systolic, was found to be 110 systolic and 90 diastolic. Her pulse rate was 90 per minute and it varied with respirations. There was no evidence of organic disease of the heart, and an electrocardiogram was reported as normal. The lungs were normal and the abdomen was soft. All muscles were flabby, yet all deep reflexes were entirely normal. There were no pathologic reflexes. All cranial nerves were functionally normal. The fields of vision and fundi were normal.

She was treated with 5 units of insulin before meals for her appetite, gelatin, 2 ounces (60 Gm.) of aminoacetic acid with meals, and rest in bed except for a ten minute sun bath daily. She was to eat everything available without restrictions, as she had been placed on a restricted diet by other doctors of medicine and cultists. She was also to have a trial with thiamine hydrochloride 50 mg. daily. Sodium amytal was to be used as a sedative if she became too much stimulated by the thiamine, as had been reported.

After two months of this treatment without appreciable benefit the parents again turned to a chiropractor.

CASE 4 (Marsh).—Dr. Clemson Marsh has reported the case of a restaurant proprietor aged 55 who had been a professional baseball player in his youth and who wore himself out in the course of two weeks of day and night work. He looked after his business in the daytime and, because of labor shortage, redecorated his place of business at night. He slept only three or four hours a night during the period of overwork but did not feel the lack of sleep. He rather reveled in his accomplishment. On the last night he worked with a linoleum polisher, moving furniture about, bending, pushing, lifting from 8 a. m. one day to 4 a. m. the next, with one-half hour for each meal and no time for rest. When he was through he remarked "If there were fifteen minutes' more work to do it would be impossible for me to do it."

After a few hours of rest he attempted to resume his regular work but was extremely weak. The weakness progressed during the following week until his arms and legs were practically useless. During this week soreness of all muscles developed. In a few more days the weakness and soreness increased until he was unable to get in and out of bed alone. His arms hung limp at his sides, and even with utmost effort he could not raise them to the shoulder level. He walked, when he was helped to his feet, with a shuffling gait.

In a month he made a trip to a spa and took baths, and the soreness subsided but he was still unable to dress himself or to shave.

He was studied by Dr. Marsh four months after the onset. There was a moderate residual tenderness of the arm and shoulder regions on palpation or on active movement. He was still unable to tie his necktie or to button his collar. There was atrophy of the deltoids and generalized loss of muscle tone. All reflexes were normal, and no fibrillary twitching was found. A biopsy of the left deltoid muscle showed normal structure. There was nothing to suggest muscular dystrophy.

He was reexamined seven months from the onset, and definite improvement was noted. He had gained 5 pounds (2.3 Kg.), but his gait was slow and faltering. He was able to raise his arms above his head. Dr. Marsh examined him again one year from the onset and found a complete recovery except for a little weakness of the arms. Note is especially made of the fact that this patient never remained in bed all day after the episode. He looked after his business in a supervisory way. Recently the patient relapsed after exertion.

Dr. Marsh also reported an observation in a medical student unused to physical exercise who climbed a mountain for four hours with experienced mountain climbers. He had fibrillary twitching in his lower limbs for six weeks afterward.

COMMENT

The syndrome is clearly due to neuromuscular exhaustion. After a prolonged period of overwork, usually over a period of months, a final spurt of severe expenditure of energy results in exhaustion approaching paralysis. During the period of overwork the mental state is one of euphoria with apparent insensitivity to fatigue until a sudden realization of exhaustion supervenes. Extreme weakness appears while a psychomotor restlessness continues, making much needed relaxation difficult. The patient attempts to keep on his feet, complaining of generalized muscular cramps and pains, which condition passes into one of flaccidity of muscles with fascicular twitching. Insomnia followed by sleep of exhaustion supervenes, from which the patient awakens with partial relief from the pain and restlessness but with paralysis. In a few weeks atrophy supervenes, while fasciculation is prominent and a loss of weight of 25 pounds (11 Kg.) or more occurs. Under rest and good food a gradual recovery is made, but the patient's former level of efficiency is not reached and focal atrophy of the muscles most severely affected remains. The atrophy is most severe (and tends to remain) in the girdle musculature rather than in the small muscles of the limbs. Temporary and possibly residual neuronal changes may occur.

The pathogenesis has not been demonstrated in terms of physiology. Each patient so far observed has not been seen until weeks had elapsed and the stage of muscular atrophy with fasciculation had developed. We

must assume that in a state of severe exhaustion a point is reached in which metabolic products accumulate in the muscles until the anabolic chemical mechanism fails. A line is crossed, as it were, beyond which muscular or neuromuscular recovery is impossible until prolonged rest and nutritional aid are given. When the line is once crossed atrophy ensues in spite of treatment, and months of relative rest are required for reestablishment of muscle physiologic function approaching the normal. Apparently the normal is never attained; the line is again reached in the future with far less expenditure of energy than was required to start the cascade the first time. The patient remains "sensitive" to overwork very much as a victim of heat stroke remains sensitive to heat.

One might speculate extensively about the chemical breakdown which results from severe muscular overwork, but it seems to me that unless experimental work is done the answer must be uncertain. In the physiology of muscular contraction it is known that the greater part of the lactic acid is produced after the contraction is over, i. e. in the recovery phase. It seems quite possible that when one contraction follows another in rapid succession and without sufficient rest to overcome the oxygen debt such accumulation may poison the muscle by upsetting the anabolic process. At any rate the cases show that, once a certain point is reached, a large part of each poisoned muscle does not recover. The muscle atrophies and disappears during a long period of fascicular twitching. When recovery does occur the muscle fibers regenerate.

I feel that the facts here presented cannot possibly be new. In times of war and in famine as well as in times of great disaster there must be large numbers of persons who succumb to neuromuscular exhaustion. It is probable that the condition fails to be widely discussed because exhaustion seems a natural cause of death under such circumstances. Soldiers who fall exhausted on a march and victims of torpedoed vessels who die of exhaustion probably present the syndrome but fail to be studied over a period of recovery lasting many months.

The cases here reported were not studied during the first weeks of the disability, when creatine must have been present in the urine. The presentation is inherently weak in this regard, but it is hoped that interest in the subject will be stimulated so that the chemistry can be worked out and rapid remedial measures developed.

SUMMARY

A syndrome not found described in the literature has been observed—neuromuscular exhaustion followed by atrophy and fascicular twitching requiring months for recovery. During a period of euphoria with oblivion of fatigue a person continues to work until he suddenly realizes complete neuromuscular exhaustion approaching paralysis. Psychomotor restlessness continues, pains and tenderness are prominent, the muscles become flabby while they twitch and atrophy; paralysis supervenes with great loss of body weight. Months are required for recovery. In most severe cases residuals remain; exacerbation may appear after relatively slight exertion. The patients are not neurasthenic; they rather ignore their disability and herein lurks danger.

727 West Seventh Street.

HEMORRHAGIC COMPLICATIONS, WITH DEATH PROBABLY FROM SALICYLATE THERAPY

REPORT OF TWO CASES

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AND
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The salicylates are usually considered to be relatively safe drugs, and reports of fatalities from their use have been rare. In the treatment of rheumatic fever, however, large doses are employed, approaching the toxic or even lethal dosage as listed in some pharmacology textbooks.[1] Minor toxic reactions, such as tinnitus, are therefore expected to occur. Coburn [2] has recently advocated the intravenous administration of large doses of sodium salicylate in the treatment of rheumatic fever. In 1 adult in whom this form of therapy was used and in an infant given relatively large doses of acetylsalicylic acid we have recently encountered death which seems to have been due to salicylate therapy.

REPORT OF CASES

CASE 1.—*History.*—A white woman aged 20, unmarried, was first admitted to Parkland Hospital on May 5, 1944 because of small ulcerations on the bottoms of her feet. Numerous small pustules were found on the feet and ankles, and a few on the thighs. These had been present for three days, and on the morning of admission there were some swelling and pain in the left ankle. Except for these findings, physical examination at this time was negative. Hot packs and local application of sulfathiazole ointment were used, and the pustular lesions cleared. The swelling and pain in the ankle disappeared in three days, at which time she was discharged from the hospital.

The morning after discharge, however, she awakened to find swelling and pain in the left ankle and also in the left elbow and wrist. She was readmitted to the hospital. She had no other complaints at this time.

She had had whooping cough and measles. Otherwise the past history was negative.

Physical examination revealed that the patient was well nourished and well developed and was not acutely ill. Her temperature was 99.2 F., pulse rate 85, respiratory rate 25. The head, eyes, ears, nose and throat were normal. Examination of the heart revealed no murmurs. The apex beat was in the midclavicular line in the fifth interspace. The lungs were clear. There was no abdominal pain or mass. There was moderate, diffuse swelling of the left wrist and slight swelling of the left ankle.

Admission laboratory studies revealed a negative Kline test. The urine had a specific gravity of 1.027, 10 mg. of albumin per hundred cubic centimeters and 4 to 6 pus cells per high power field. The red blood cell count was 4,850,000, hemoglobin 14 Gm. and the total white blood cell count 7,300. The differential count revealed 1 band, 62 segmented cells and 37 lymphocytes. The sedimentation rate was 18 mm. in one hour. Throat culture yielded Staphylococcus albus and the alpha streptococcus. An electrocardiogram taken on the day of admission showed no deviation from the normal.

It was thought that the patient had acute rheumatic fever, and 10 Gm. of sodium salicylate was given intravenously on the day following admission. It was given in 1,000 cc. of isotonic solution of sodium chloride, 30 drops per minute. This was repeated on the next day, May 10. On this day the joint pain was much improved. On May 11 sodium salicylate

From the Department of Pathology, Southwestern Medical College, and the Children's Medical Center.

1. Sollmann, T.: A Manual of Pharmacology, Philadelphia, W. B. Saunders Company, 1942.

2. Coburn, A. O.: Salicylate Therapy in Rheumatic Fever: A Rational Technique, Bull. Johns Hopkins Hosp. **73**: 435 (Dec.) 1943.

was given by mouth; a total of 10 Gm. was administered, and this regimen was followed for the succeeding four days. On May 12 she had had complete clearing of joint swelling and pain. On this day she had some tinnitus.

On May 15, seven days after admission, she became irrational and manifested paranoid ideas. She had several outbursts of crying and exhibited periods of tachypnea and hyperpnea. These periods were followed by profuse perspiration and cyanosis. Her temperature had been normal until May 15, when it gradually rose to 102 F. The next day her temperature was 106.4 F. at 8 a. m. The pulse rate rose to 120, and respirations varied from 25 to 45 per minute. She continued irrational. The blood pressure fell on several occasions to as low as 80/40. She was given a transfusion of 500 cc. of blood and also 35 Gm. of plasma in four times concentrated form. Her blood pressure rose to 100/40. The temperature dropped to 102 F. during May 16.

A blood culture taken on May 10 was negative. Urinalysis on May 16 revealed 1.023 specific gravity, acid reaction, 325 mg. of albumin per hundred cubic centimeters, negative sugar, 4 plus acetone, 5 pus cells and 300 red cells per high power field, with many finely and coarsely granular casts in the centrifuged sediment. On May 16 the red blood cell count was 3,650,000, hemoglobin 9.5 Gm. and total white blood cell count 11,050. The differential white blood cell count revealed 9 band cells, 77 segmented cells, 6 lymphocytes and 8 monocytes. Blood urea nitrogen was 45 mg. and sugar 128 mg. per hundred cubic centimeters. The carbon dioxide combining power was 46 volumes per cent. She continued to be irrational, with hysterical outbursts and periods of hyperpnea, cyanosis and perspiration. On May 16 a consultant's note read "This patient presents a bizarre picture with flaccid paralysis and absent reflexes but none of the usual signs of meningeal irritation. The sudden hyperthermia last night is difficult to explain except on the assumption of a lesion of the nervous system. From the clinical findings, encephalitis of some peculiar type is the most likely diagnosis." A lumbar puncture was done and spinal fluid described as turbid obtained. However, there were no white

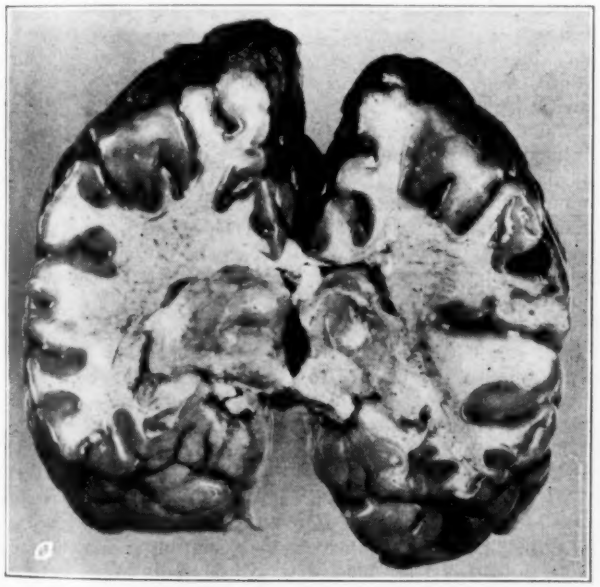

Fig. 1 (case 1).—Section through the brain at the level of the thalamus and the hypothalamus, showing petechiae in gray and white substance.

cells or red cells in the fluid. The protein content was 35 mg. per hundred cubic centimeters, the Wassermann reaction negative, the colloidal gold curve negative and smear and culture negative.

She became comatose and died at 3:35 a. m., May 17.

Autopsy.—This was performed five hours after death. The body weight was 105 pounds (48 Kg.), the height 5 feet 2 inches (157.5 cm.). The only significant external observations were hemorrhages in the cubital fossae at the sites of venipuncture marks and petechiae over the arms and back. There were reddish blue areas of hemorrhage scattered throughout the parietal and visceral peritoneum and mesentery of the small intestine.

There were a few petechiae in the pericardium; otherwise the heart was normal. The right lung weighed 730 Gm. and

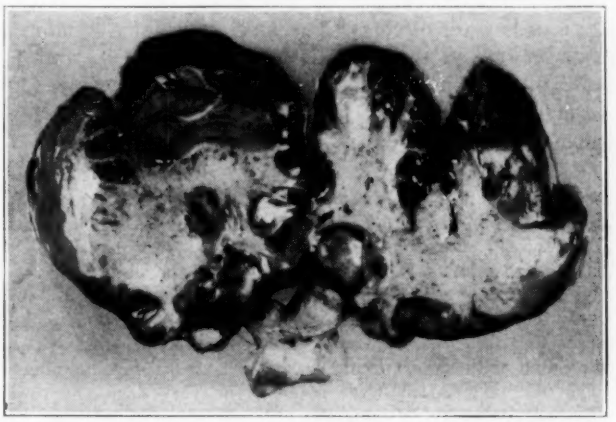

Fig. 2.—The cerebellum in case 1; numerous petechiae scattered throughout.

there were large bluish red hemorrhagic areas scattered throughout all lobes. The same was true of the left lung, which weighed 645 Gm. There was moderate edema in the remaining lung tissue. The liver weighed 930 Gm. and had a yellow gray mottled appearance. A few petechiae were noted in the pancreas. The kidneys were hyperemic. The gallbladder, spleen, adrenals, urinary bladder, uterus, cervix, fallopian tubes and ovaries were essentially normal. Many large bluish hemorrhagic foci were found scattered throughout the retroperitoneal tissues. The gastrointestinal tract was normal.

There was a small subdural hemorrhage about 1.5 cc. in volume located over the anteromedial portion of the right cerebrum. The entire brain externally and on section was pinker than normal. Multiple coronal sections through the brain revealed many petechiae less than 1 mm. in size, for the most part, in the cerebrum (fig. 1) basal ganglions, thalamus, hypothalamus, pons, medulla, substantia nigra, red nucleus, cerebral peduncles and the cerebellum (fig. 2). The brain weighed 1,250 Gm.

The spinal cord was found to have a few scattered petechiae throughout its entire length.

Microscopic Examination.—Sections from all the brain areas mentioned revealed intense capillary dilatation. There were many recent interstitial and perivascular small hemorrhages in these sections (fig. 3). In some of the larger areas of hemorrhage, focal encephalomalacia was noted. There was no evidence of any inflammatory reaction.

Petechial hemorrhages were found also in sections of heart (epicardium), large and small intestine, skin of the back and mesenteric adipose tissue.

Acute hyperemia was noted in the liver, spleen, pancreas and kidneys.

The liver showed hydropic and parenchymatous degeneration.

Sections of lungs revealed extensive acute hyperemia and diffuse recent alveolar hemorrhage (fig. 4). There was excessive accumulation of polymorphonuclears in some areas of hemorrhage.

Sections of synovial tissue of the left ankle showed no abnormalities.

Bacteriology.—Culture of the splenic pulp was negative.

Summary.—The principal pathologic diagnoses were pronounced petechial hemorrhages throughout brain, many diffuse hemorrhages in the lungs, petechial hemorrhages in the peritoneum, mesentery, retroperitoneal tissues, pericardium, spinal cord, pancreas, large intestine, small intestine and skin, small

subdural hemorrhage over the right cerebrum, much generalized acute passive hyperemia, early bronchopneumonia of both lungs, and hydropic and parenchymatous degeneration of the liver.

The close correlation between the administration of sodium salicylate and the onset of mental symptoms, hyperpyrexia and hyperpneic attacks suggest that the clinical findings might be explained on the basis of toxic salicylate effects. The absence of any inflammatory lesions in the central nervous system at autopsy and the finding of generalized acute hyperemia and focal hemorrhages are further indications that this was the case.

CASE 2.—*History.*—A Negro boy aged 4 months was admitted to Parkland Hospital on June 11, 1944 because of fever and deepened respirations. The child was well until about three days before admission, when he developed a mild cold. One day before admission the mother thought the child had fever and she gave it half of an acetylsalicylic acid tablet (0.17 Gm.) every four hours for four doses and also gave mild protein silver in castor oil as nose drops. The child seemed to be about the same until approximately twelve hours before admission, when the respirations were noted to be very deep and rapid. This continued until admission at 5:30 a. m. The baby had had no diarrhea, cough or other symptoms.

The child was a full term delivery, with uncomplicated labor and had had no previous illnesses or immunizations.

Physical examination showed that he was well developed and well nourished. His respirations were very deep and rapid and he was apparently unconscious. The temperature was 102 F., pulse rate 120, respiratory rate 45. The head was normal in size, but there was pronounced craniotabes. The anterior fontanel was soft. The ear drums were mildly injected. The mouth was negative but the throat was slightly generally reddened; no membrane was present. Respiration was heaving in type,

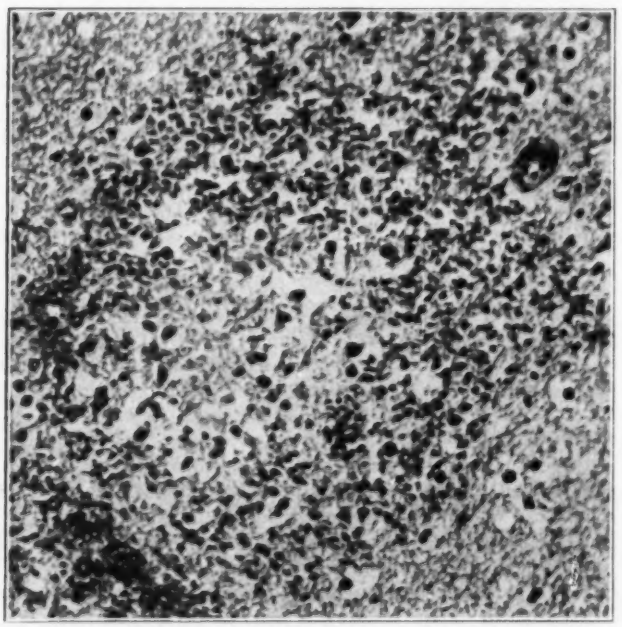

Fig. 3 (case 1).—Microscopic appearance of a hemorrhagic lesion in the white substance of the cerebellum. Early encephalomalacia is present. Magnification 200 diameters.

but there was no chest retraction. The breath sounds were harsh, but no rales were present. The heart was normal in size to percussion. No murmurs were heard. There were beaded prominences along all the costochondral junctions. The abdomen was normal and the genitalia were normal. The skin was hot to touch around the head and trunk, while the extremities were cold. The extremities were relaxed and the reflexes depressed.

A catheterized urine specimen showed acetone 4 plus, sugar negative. An x-ray examination of the chest revealed patchy areas of increased density throughout both lung fields.

With air hunger type of respirations and 4 plus acetone, the child was thought to be in a state of acidosis; 220 cc. of lactate-isotonic solution of three chlorides was given intravenously and 250 cc. subcutaneously. The temperature rose to 106 F., and half of an acetylsalicylic acid tablet (0.17 Gm.) was given on

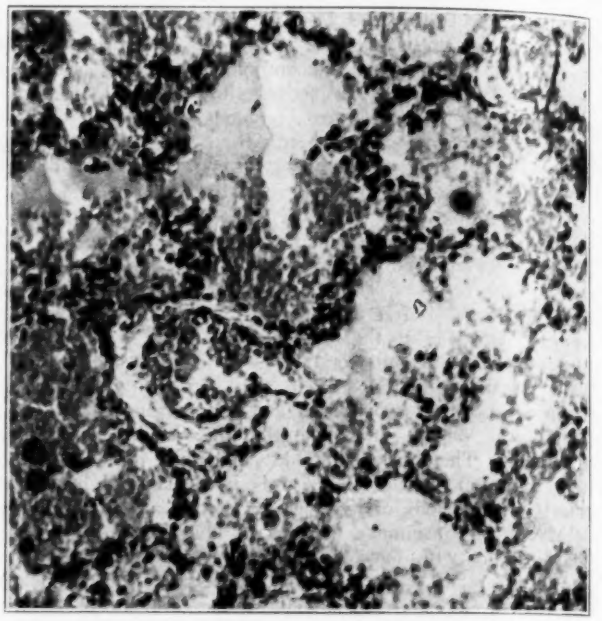

Fig. 4.—Microscopic appearance of lung in case 1. There are pronounced recent hemorrhage and edema in the alveoli, and acute hyperemia in the alveolar capillaries. Magnification 200 diameters.

two occasions and also cool sponges. Sulfathiazole was administered, 0.5 Gm. as the initial dose and 0.25 Gm. every four hours. At 11 a. m., five and one-half hours after admission, the child began having severe generalized convulsions, with which respirations became very poor. A lumbar puncture revealed, at this time, clear fluid, with no increase of pressure. Sodium phenobarbital 0.23 Gm. was given slowly, intravenously, until the convulsions were quieted. Oxygen was given by inhalation. The respirations became very slow, 6 to 10 per minute, in spite of nikethamide, caffeine and epinephrine. Six hours later, however, the child seemed to be improved, with regular respirations and only slight cyanosis. However, a few minutes later respirations dropped to 4 to 6 per minute and about one hour later the child died from respiratory failure, twelve hours after admission.

Autopsy.—This was performed two hours after death. The body weighed 14 pounds 10 ounces (6.6 Kg.). Pronounced craniotabes and beading of the costochondral junctions of the ribs were noted to be present.

The trachea and main bronchi contained a small quantity of a thick greenish fluid resembling stomach contents. The right lung weighed 35 Gm. and the upper lobe was dark purple, firm and airless. It exuded bloody fluid on pressure. The middle lobe was air containing and the lower lobe was mottled by collapsed blue, dry, airless areas. The left lung weighed 25 Gm. and on section revealed diffusely red but air containing parenchyma. The bronchi of this lung contained a small amount of greenish mucoid fluid, apparently stomach contents.

The liver weighed 250 Gm. and appeared normal. The heart, thymus, gallbladder, spleen, pancreas, adrenals, kidneys, urinary bladder, prostate, testicles and epididymides, gastrointestinal tract and neck organs were normal.

The mesenteric lymph nodes seemed to be enlarged, varying from 0.5 to 1.5 cm. in size.

The meninges were clear. Externally and on section throughout the brain many dilated small vessels were seen. Only in

the hypothalamus could additional changes be seen with the naked eye. Here there were numerous, very tiny, pinpoint hemorrhages in the brain substance.

Microscopic Examination.—Sections of the brain revealed very pronounced acute hyperemia everywhere in the brain substance and in the leptomeninges. There were noted numerous small, recent, perivascular and interstitial hemorrhages in a section of the hypothalamus (fig. 5); a few were also noted in the medulla, just underlying the floor of the fourth ventricle, and one such small hemorrhage was present in the medulla of the cerebellum. In the brain tissue adjacent to some of these hemorrhages there was slight myelin degeneration.

A section of the upper lobe of the right lung revealed pronounced acute hyperemia, edema fluid of high protein content, and extensive diffuse, recent, intra-alveolar hemorrhage (fig. 6). There was no inflammatory reaction. Elsewhere in the lung, sections showed hyperemia, slight edema, small alveolar hemorrhages and focal atelectasis. The alveoli of most sections contained a greenish granular precipitated material.

In a section of heart a small epicardial petechial hemorrhage was found.

The liver was found to be the seat of fatty degeneration of advanced degree. There were hyperplasia of the splenic pulp and also slight lymphoid hyperplasia of a mesenteric lymph node.

There was acute hyperemia in the adrenal medulla, in the kidneys and in the large and small intestines.

Sections of the stomach, thymus, larynx, tongue, tonsil, thyroid, parathyroid, esophagus, gallbladder, testicle, epididymis and prostate were all essentially normal.

Bacteriologic Examination.—Cultures of the upper lobe of the right lung and of splenic pulp were negative.

The main pathologic diagnoses were petechial hemorrhages in the hypothalamus, medulla and cerebellum, extensive hemorrhage in the right lung, petechial hemorrhage of the epicardium,

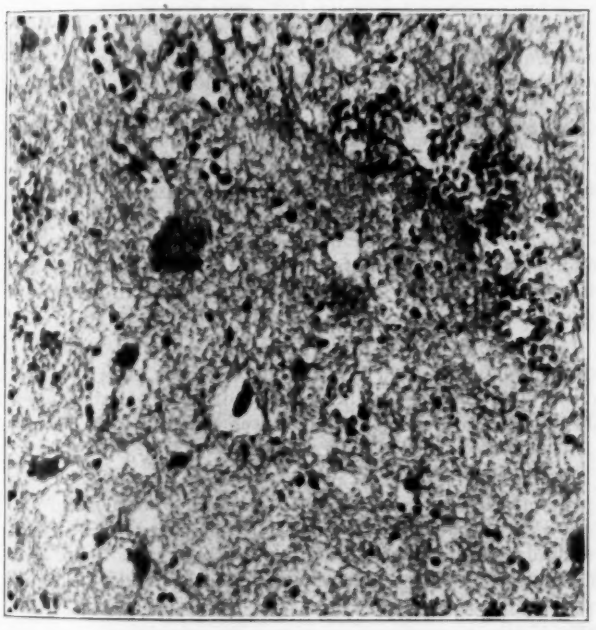

Fig. 5 (case 2).—Microscopic section of region of hypothalamus showing recent petechiae. Magnification 200 diameters.

edema of the lungs, pronounced acute hyperemia of the brain, lungs, kidneys, adrenal medulla and large and small intestines, focal atelectasis of the lungs, aspiration of stomach contents and rickets.

The hyperpnea, hyperpyrexia and convulsions seemed to follow the comparatively large doses of acetylsalicylic acid, and the failure to demonstrate an inflammatory disease at autopsy makes it likely that these toxic effects of salicylates were the cause of death. The dosage given is well above the toxic dose according to Barnett, Powers, Benward and Hartman.[3]

COMMENT

Previous reports of deaths due to salicylates have not emphasized hemorrhagic complications. Rapoport, Wing and Guest[4] suggested that the hemorrhagic

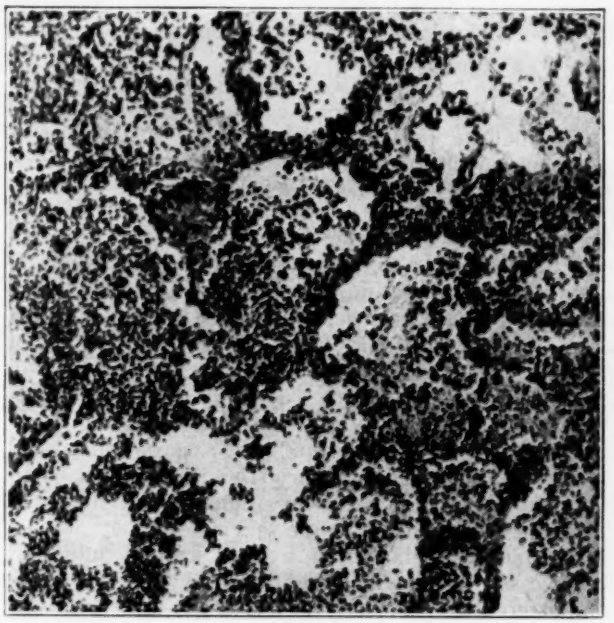

Fig. 6.—Microscopic section of the lung in case 2. There is very evident hyperemia. The alveoli are filled with red blood cells and some edema fluid. Magnification 200 diameters.

tendency of some cases of rheumatic fever might be explained on the basis of the salicylate therapy. Stevenson[5] reviewed the cases of poisoning from methyl salicylate and reported 3 cases of his own. There were 43 such cases. About half of the 13 cases in which autopsy was performed showed petechiae in the epicardium, and almost one third hemorrhages in pleura and lung. In none was a generalized hemorrhagic disease present, however.

Hypoprothrombinemia has been shown by Link and others[6] to occur in rats which have received salicylates. These authors pointed out the similarity that exists between the salicylate radical and dicumarol, a strong hypoprothrombinemic agent. Meyer and Howard[7] and Rapoport, Wing and Guest[4] also produced hypoprothrombinemia in animals and in human beings with therapeutic doses of salicylates. It was shown that vitamin K prevented this hypoprothrombinemia, so that it is likely that the hypoprothrombinemia is not due to the liver damage. However, Lutwak-Mann[8] showed that the liver glycogen disappeared following salicylate

3. Barnett, H. L.; Powers, J. R.; Benward, J. H., and Hartman, A. F.: Salicylate Intoxication in Infants and Children, J. Pediat. **21**: 214 (Aug.) 1942.

4. Rapoport, S.; Wing, M., and Guest, G. M.: Hypoprothrombinemia After Salicylate Administration in Man and Rabbits, Proc. Soc. Exper. Biol. & Med. **53**: 40 (May) 1943.

5. Stevenson, C. S.: Oil of Wintergreen (Methyl Salicylate) Poisoning: Report of 3 Cases, One with Autopsy, and a Review of the Literature, Am. J. M. Sc. **193**: 772 (June) 1937.

6. Link, K. P.; Overman, R. S.; Sullivan, W. R.; Huebner, C. F., and Scheel, L. D.: Studies on the Hemorrhagic Sweet Clover Disease: XI. Hypoprothrombinemia in the Rat Induced by Salicylic Acid, J. Biol. Chem. **147**: 463 (Feb.) 1943.

7. Meyer, O. O., and Howard, B.: Production of Hypoprothrombinemia and Hypocoagulability of the Blood with Salicylates, Proc. Soc. Exper. Biol. & Med. **53**: 234 (June) 1943.

8. Lutwak-Mann, C.: The Effect of Salicylate and Cinchophen on Enzymes and Metabolic Processes, Biochem. J. **36**: 706 (Dec.) 1942.

therapy. It is of some interest that in the 2 cases reported here degenerative changes were noted in the liver.

The severe generalized hyperemia in our 2 cases suggests the possibility of some capillary damage by the salicylates. The petechial hemorrhages can readily be explained on the basis of severe hyperemia with accompanying hypoprothrombinemia.

Tachypnea and hyperpnea in salicylate poisoning have been explained on the basis of fixed acid acidosis.[9]

In addition to the 2 cases reported here, Fashena and Walker have recently observed another case of nonfatal acute salicylate poisoning occurring in the course of treatment of rheumatic fever. This case was studied from the clinical and chemical standpoint.[10]

SUMMARY

Although severe toxic reactions following salicylate therapy are uncommon, the recent interest in more intensive forms of salicylate therapy renders the report of 2 cases of probable fatal salicylate poisoning of interest.

The outstanding findings at autopsy were hemorrhagic changes, widespread over the body but particularly involving the brain, and severe widespread hyperemia. The explanation of these findings is probably a combination of capillary damage and hypoprothrombinemia produced by the salicylates.

It would seem that vitamin K is strongly indicated in all cases in which large doses of salicylates are administered.

THE USE OF THE SULFONAMIDES IN PYELONEPHRITIS IN PREGNANCY

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BOSTON

Introduction of the sulfonamide drugs into general use produced a radical alteration in the management of infections in pregnancy. The test of their effectiveness will rest on a survey of the condition of patients so treated after the lapse of five or more years after the illness with which the injury began. No adequate surveys have been made to date. A yardstick for comparison with similar cases treated by previous methods already exists. Such surveys are apt to follow soon after cessation of hostilities, when sufficient man power becomes available for their prosecution. Meanwhile those in whose hands the care of such infections rests have attempted to determine essential requirements for maximum efficiency in the use of these drugs. This communication is limited to a statement of policy of the Boston Lying-in Hospital, with some observations on the already obvious deficiencies of present practices and inadequacies of the drugs employed.

Optimism based on apparent cures of urinary infections in pregnancy following delivery which permitted uncured infections to persist and result in major degrees of damage to renal tissue and efferent channels in subsequent years has a corollary in the sulfonamide era when prompt subsidence of symptoms and the production of a high percentage of cures tends to be accepted by those in charge as indicative of cure in all. This concept is still further magnified since bladder symptoms often remain mild or absent until retrogression of pregnancy changes has taken place at the end of weeks or a few months, at which time obstetric care has often ended. This leaves a certain number of uncared for women in whom infection persists for years. Surveys of pyelonephritis in all types of patients indicates that recurrent and persistent infections appear to be more potent in production of major degrees of remote damage than can be ascribed to the acute stages of infection with which the illnesses begin. That concept remains tenable in the sulfonamide era. It is not to be construed as indicating that minimizing the severity of the initial infection and limiting its duration do not soften the blow. This has been made possible by the sulfonamides.

REPORT OF CASES

CASE 1.—*History.*—Mrs. E. C., aged 30, mother of two children, had a short attack of pyelonephritis involving the right kidney eight years ago during her first pregnancy. It was severe while it lasted. It is presumed from the subsequent history that cure was not produced. Two years later she was given sulfanilamide for bladder symptoms. Six years ago she had paralysis, involving her bladder, due to encephalitis, from which she appeared to recover entirely within a few months. Two years ago she had a second pregnancy in which severe pyelonephritis symptoms confined to the right kidney developed early in the gestation. In spite of repeated courses of sulfadiazine and sulfathiazole there were frequent recurrences of fever and pain in the right kidney. The urine was never clear. All symptoms seemed to subside after delivery. About three months after delivery both the renal pain and bladder frequency returned and have been troublesome since that time.

Examination.—There was no remnant of paralysis. There was tenderness over the right kidney but no mass. The urine showed pus and many bacilli.

Cystoscopy.—There was no bladder residual. The mucosa was chronically inflamed. Both ureteral orifices appeared normal except for edema. There was a residual urine of 15 cc. in the right pelvis. The urine was cloudy, as was that in the bladder. The urine from the left kidney was clear. Phenolsulfonphthalein excretion from both kidneys was prompt and of good concentration and approximately equal from the two kidneys.

Pyelography.—The use of the retrograde method showed a normal pelvis and ureter on the left. On the right there was considerable dilatation of the pelvis and the whole of the upper third of the ureter. The lesion was not characteristic of a congenital defect and was of ureteritis.

Treatment.—A series of ureteral dilations were done. These produced neither diminution in the residual urine nor improvement in the appearance of the pelvis and ureter. These were followed by two courses of six days each of sulfadiazine. One of these appeared to produce normal urine, but infection was present two weeks later; the other made no improvement in the urine at all.

It is almost certain that nephrectomy will eventually be required. While there is no pyelography available previous to child bearing there is no urinary history either relating to childhood or early adult life up to the time of conception.

CASE 2.—*History.*—Mrs. P. S., aged 28, was examined by intravenous pyelography two years before marriage because of symptoms which were finally diagnosed appendicitis. The report from that examination (the films were not seen by me) described the kidneys as normal in appearance and function. Five years

9. Johnson, C. C.: The Salicylates: XIX. The Question of Acidosis Following Administration of Salicylates, J. A. M. A. **94**: 784 (March 15) 1930.

10. Fashena, Gladys J., and Walker, J. N.: Am. J. Dis. Child., to be published.

From the Urological Clinic of the Boston Lying-in Hospital.

Read before the joint meeting of the Section on Obstetrics and Gynecology and the Section on Urology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 16, 1944.

ago the patient had pyelonephritis in the fifth month of her first pregnancy. Labor was induced after sulfanilamide therapy had failed to produce subsidence of symptoms. Intravenous pyelography, also from the report of the x-ray department in a neighboring hospital, showed only a minor degree of renal dilatation. All symptoms subsided promptly after abortion. There was no evidence as to whether she then became free of infection. At any rate she remained free from symptoms of any kind for two years. At that time right sided pain developed for which her appendix was removed without relief. There was no frequency of urination, although reference to the record of the hospital in which the operation was done showed her to have had infected urine at the time of appendectomy.

Two years ago she again became pregnant. The right sided pain became worse during the first months of pregnancy but ceased about the fifth month. Fever, never of severe degree, appeared between the fifth and sixth months of gestation, for which she had repeated courses of sulfathiazole. These treatments produced afebrile periods but did not clear the urine of bacteria. They ceased after delivery.

The right renal pain was absent for about one year after delivery of the second child. After that date it returned with greater severity than at any time previously. There were no fevers with these attacks.

Examination.—This elicited some tenderness in the right renal region, but there was no mass. The urine showed a few pus cells and many bacteria.

Cystoscopy.—There was no bladder residual, although the supports of the bladder were weakened on the left side and there was pouching. There were chronic inflammatory changes throughout the bladder mucosa. There was a residual urine of 8 cc. in the right pelvis but none in the left. The urine from the right pelvis was cloudy and from the left clear. Cultures from the right showed bacilli and from the bladder also, but that from the left showed no growth.

Pyelography.—The intravenous method showed dye appearing in both pelves at five minutes, with the greatest concentration of the dye at fifteen minutes on the left but at forty-five minutes on the right. There was residual urine in the right pelvis at the end of one hour. A film of the bladder after voiding showed no bladder residual.

Treatment.—After a series of five ureteral dilations with number 9, 10 and 11 bulbs the residual urine in the pelvis was 2 to 3 cc. in amount. Sulfadiazine therapy for six days produced negative cultures. During three months while the patient was under observation there was neither further renal pain nor a return of the infection. She will be observed at six month intervals.

PRESENT POLICY OF SULFONAMIDE THERAPY

Treatment of urinary infections during pregnancy are carried out in both outpatient and house cases. There seem to be no contraindications to treating some patients in the outpatient department. Those so treated are patients without fever in whom evidence, through catheter urines, is found of either pus or bacteria or both. Since most of our patients are a controlled group, are on increased fluid intake during pregnancy as a part of hospital policy and are seen regularly in antepartum clinics and at home if in trouble, the majority of admissions of infected patients are through the outpatient department. Some of these have had no symptoms of any kind and the finding of infection has been through routine examination of urine. In others, after a day or two of mild urinary symptoms at home, the patient has been seen by the district nurse and the house officer and sent to the outpatient department as soon as temperature is normal. Increased fluid intake is thought to be responsible for the mildness of symptoms in these cases. As outpatient cases they receive sulfathiazole or sulfadiazine in 2 gram doses daily for six days with 60 grains (4 Gm.) of sodium bicarbonate three times daily. The fluid intake is kept at 2,500 to 3,000 cc. of water in addition to other fluids. If they become febrile while under outpatient treatment they are referred as house cases. A few febrile patients are admitted through reference by physicians and our own house staff directly to the hospital.

Febrile patients in the hospital are treated less routinely and more in accord with their condition at admission. Emphasis is placed on alkalization of the urine and obtaining adequate fluid intake as the first measure of treatment even though it means delay in instituting antisepsis. A fluid intake even in a desiccated patient of 3,500 to 4,000 cc. and sufficient alkali to meet the demands for alkalinity of the urine is usually obtained within six to twelve hours after admission. As soon as this is accomplished, sulfadiazine or sulfathiazole is started. The initial dose is commonly 4 Gm. for the first day and 2 Gm. daily for the next five or six days. Seldom is drug therapy continued beyond that period at one time even if cure is not accomplished. If the acute symptoms do not subside we prefer to keep the patient on high fluid intake and resume treatment at a later time after some degree of tolerance for infection has been acquired. Complications from the drug appear to be commonest in protracted therapy and, in addition, further treatment adds little to the chance of clearing the infection. There is also virtue in awaiting development of antibodies by the patient. Under this regimen we find little use for intravenous administration of the drugs.

The degree of dilatation of pelves and ureters which patients develop appears to bear little relation to efficacy of therapy except in extreme instances of atony and distention of the pelves and ureters. The following histories are illustrative:

CASE 3.—Mrs. A. J., a quintipara aged 33, had previous pregnancies in 1935 and 1936 in another hospital and in 1938 under her own physician's care which were all uncomplicated. A miscarriage occurred at two months in 1941. This miscarriage was followed by dilation and curettage. She was now in the sixth month of gestation.

Urinary findings and not symptoms indicated her condition. The blood pressure ranged from 120/70 to 132/80. Albumin was 2 plus, and there were some red blood cells and a few casts in addition to many bacilli and 5 to 10 pus cells noted in the urine. She was considered to have both preeclampsia and urinary infection and was referred to the hospital for medication.

Intravenous pyelography showed a moderate degree of dilatation of the right ureter and pelvis but only a small degree of change in the left ureter and pelvis.

Treatment was for but five days with sulfadiazine 2 Gm. daily with sodium bicarbonate but with a fluid intake limited to 1,000 cc. in deference to her preeclamptic state. The urine cleared of pus, bacilli and blood, but there remained albumin and a few casts.

CASE 4.—Mrs. W. C., a tertipara aged 27, had her first pregnancy without complications in 1939. She had retention of urine post partum. The resulting cystitis was cleared in seven days with 80 grains (5 Gm.) daily of sulfanilamide. The second pregnancy was uncomplicated. The urine remained normal throughout the whole of gestation and the puerperium.

Gross hematuria marked the onset of pyelonephritis in the fifth month of the fourth pregnancy. The organism was a

bacillus. There was no fever by the third day of bleeding when treatment was instituted.

Intravenous pyelography showed pronounced dilatation of the right pelvis and upper ureter. There were but small degrees of change in the left pelvis and ureter. Both the bleeding and the infection cleared on six days of treatment with 2 Gm. daily of sulfadiazine with sodium bicarbonate on an intake of 2,500 cc. of fluid daily.

She finished her pregnancy without further infection or bleeding.

Patients who fail to clear under routine therapy receive further investigation except when they are near to term and free from symptoms. In the latter cases intravenous pyelography is usually done to exclude renal conditions which might complicate delivery. Such patients occur in both the outpatient and the house groups.

Debility, of which anemia is the commonest cause but which may also be the result of overwork, undernourishment or poor toleration of pregnancy, is a common cause for failure of treatment. Such patients under appropriate treatment for anemia, dietary care and social service may readily clear of infection when treated at a later time.

Acquired tolerance for infection may account for some patients who are easily cured as outpatients after having failed to become clear of infection when treated during their febrile stages as house patients. The intervals between courses of therapy is commonly two to three weeks. A few patients have been noted who were discharged from the hospital after antisepsis with both bacteria and pus still present in their urines who appeared to clear spontaneously in the interval.

Sulfonamide resistant bacteria are usually assigned a role in certain patients who resist cure. It is not easy to assess this factor. In some patients it is not possible to diminish symptoms or cure infection. These cases account in part for the rare instances of interruption of pregnancy for therapeutic reasons. We have made use of succinylsulfathiazole in 18 gram doses daily over periods of two to three weeks with but limited success.

Gross pathologic changes are responsible in the majority of patients who fail to clear under treatment. Not all degrees of abnormality defeat therapy.

Case 5.—A primipara aged 19 was admitted to the hospital because of rise in blood pressure to 180/138. Urinary infection was discovered on admission. Diagnosis was preeclampsia grade 1. The patient was kept in bed, fluids were limited to 1,500 cc. daily and 2 Gm. of sulfadiazine was administered with sodium bicarbonate 60 grains (4 Gm.) daily for six days. The infection cleared and the blood pressure fell to 120/74 in the eleven days of her stay in the hospital. An intravenous pyelogram showed the left kidney to be unrotated and moderately hydronephrotic. She continues in the outpatient department with a clear urine and a reasonable blood pressure.

Case 6.—A tertipara aged 25 had no history of urinary infection preceding her first pregnancy in 1939. She had had pyelonephritis in pregnancy at home in the care of her own physician from May to August. Her urine was very purulent, but she was then afebrile. She was admitted directly to the hospital because due. No pyelography was done before delivery, which was made immediately on admission. Delivery was followed by retention of urine and postpartum pyelonephritis. She was given 60 grains (4 Gm.) daily of sulfanilamide for twenty-four hours, then 40 grains (2.6 Gm.) daily for six days. In the meantime she was kept on constant drainage. The urine was still clear of infection when last seen after that pregnancy and puerperium in the sixth month after delivery. Her second pregnancy was in 1942. The urine remained normal throughout the whole of this pregnancy and puerperium. In her third pregnancy, while under supervision in the outpatient department, infection appeared in the sixth month. The urine became very purulent but she remained afebrile. The urine did not clear on 2 Gm. of sulfadiazine daily for six days. Retrograde pyelography showed her to have a double right kidney, the upper half of which was hydronephrotic. She remains infected but afebrile. She is due for corrective surgery after delivery.

Case 7.—A primipara aged 18, without urinary symptoms at any time in her life previous to pregnancy, was discovered to have bacilluria during the third month of gestation. The urine did not clear under 2 Gm. of sulfadiazine with sodium bicarbonate daily for six days administered in the outpatient department. This course was repeated in two weeks. Intravenous pyelography showed extensive dilatation of both pelves and ureters throughout their upper two thirds and large dilatations of the lower portions near to the bladder. There is no evidence of renal insufficiency, she remains afebrile and there is little pus in the urine, although bacilli are abundant. She continues in pregnancy under careful observation especially for evidences of renal insufficiency. It is possible that interruption may become necessary before her pregnancy is finished. She is to have urologic treatment after delivery.

In the latter cases important urologic findings may be missed to the detriment of the patient in later life. Intractable infections are apt to occur in them in subsequent pregnancies and the gross lesion be discovered at that time. In instances in which there are extensive alterations from the normal which are brought to notice for the first time through the onset of infection, interruption of the pregnancy may be necessary. Interruptions of pregnancy for urinary causes alone, eliminating those patients who have both urinary infection and another condition such as preeclampsia, now result in an average of but one abortion per year in a clinic in which from 4,000 to 5,000 deliveries are cared for.

Intravenous or retrograde pyelography is not employed for all patients who have urinary infection. It is routine for all lone kidney patients, those with histories of renal stone and hydronephrosis, those with infections already present at the beginning of pregnancy, cases of renal tuberculosis and all who have had renal surgery. Beyond these routine cases it is employed for all patients who do not clear their infections under treatment, who show gross hematuria or who present unusual initial symptoms.

Urinary infections are frequent complications of other conditions the nature of which necessarily modifies therapy for the infectious process. These are heart disease, diabetes and preeclampsia. Because of the undesirability of forcing fluids in preeclampsia and cardiac decompensation, antisepsis with limited fluids is sometimes necessary. In spite of strict limitation of fluids during treatment in these cases and large doses of the sulfonamide drugs, which are administered in pneumonia and uterine sepsis, there has not been to date any case of blockage of the urinary channels with crystals such as has become common in the nonpregnant. The patients treated in obstetric hospitals are either pregnant or recently pregnant patients whose urinary channels still exhibit some degree of modification due to the pregnant state.

Progress in management of diabetes in pregnancy has made possible treatment of these patients by almost the same routine as that for nondiabetic patients with equally good results. Preeclampsia is the most com-

monly encountered complication of infections in the urinary tract. The combination of these two diseases accounts for interruption or abortion in about 4 cases to 1 for uncomplicated urinary infection. Sulfonamide therapy appears to do no harm to patients with toxemia who do not have nitrogen retention.

Since the introduction of the sulfonamide drugs, renal inadequacy from severe pyelonephritis appears to have been eliminated. If the infection cannot be cured in these cases, it can almost always be rendered asymptomatic and the acute involvement of the renal parenchyma greatly reduced in severity. When renal inadequacy is encountered nowadays one should suspect gross pathologic change in the kidneys.

Cystoscopy for pyelonephritis in pregnancy is now much less frequently employed than before the sulfonamides. There are a few patients in whom lavage of the pelves to remove massive purulent material is beneficial either before or during treatment with the sulfonamides, but this procedure is now essentially diagnostic. Most kidneys in pregnant women have sufficient renal substance to permit self clearance if adequate fluid intake is provided, without resorting to artificial means.

Except in obstructive ureteral calculus, renal and ureteral stones are reasonably well tolerated when the severity of the attending pyelonephritis is minimized by the sulfonamides. In obstructing calculi it is sometimes possible to manipulate the calculus cystoscopically and provide drainage. Stone is now most commonly treated surgically after delivery.

SUMMARY

The sulfonamide drugs have greatly modified the management of pyelonephritis in pregnancy for the better. Determination of the exact degree of benefit which these drugs have made possible cannot be made until surveys of patients at from five or more years from the time of infection have been compiled.

Sufficient experience has been accumulated to indicate that the beneficial effects of these drugs in ameliorating symptoms can be expected to take place in almost all patients whether or not cure of the infection is accomplished. A high percentage of patients have their urines rendered sterile both in uncomplicated cases and in those with complicating diseases, and with safety to the patient.

Among the uncured cases are some in which persisting infections are producing extensive damage to the efferent channels and can be expected to do so eventually to the renal cortex similar to those shown in surveys of patients from the previous regimens. These are preventable.

There are two major defects in obstetric practice as I see the problem in relation to pyelonephritis. One is failure to investigate urologically those patients who do not obtain cure through sulfonamide therapy for detection of gross pathologic conditions. The other is that many women leave obstetric care with urines still infected from which, in subsequent years, through long continued or repeated acute injuries, preventable gross damage to the urinary tract results.

Optimism based on apparent cures of pyelonephritis in pregnancy following delivery which was responsible for the high percentage of abnormal urinary tracts found after five or more years in the presulfonamide era has its corollary in the sulfonamide era when prompt subsidence of symptoms appears to be mistaken for cure. Similar cases to those already described in previous reports are occurring in sulfonamide treated patients. Let us hope that surveys will show that the number of such cases is greatly reduced in comparison with published end results.

99 Commonwealth Avenue.

ABSTRACT OF DISCUSSION

DR. J. P. GREENHILL, Chicago: The word pyelitis is commonly used for the subject under consideration, but, as indicated in Dr. Crabtree's title, there is damage to the kidney in most cases; hence the correct term is pyelonephritis. Likewise the ureter is generally involved, so there is really a pyelonephritis and ureteritis. There is a tendency for so-called cured or relieved pyelonephritis to flare up during the puerperium in at least half the cases. If the urinary infection is present longer than three months after delivery it is almost certain that there is a gross pathologic condition present and a complete study of the urinary tract must be made. Even if the infection is cleared up, a complete study of the urinary apparatus should be made before a new pregnancy is planned, because a woman who has had pyelonephritis in one pregnancy has about one chance in four of developing this complication in a subsequent pregnancy. Contrast this with the usual incidence of pyelonephritis in pregnancy of 1 in 50 cases. If a new pregnancy begins before the urinary infection is cleared up, the chances of recurrence are one in two. Many women have permanent defects such as hydronephrosis and hydroureter following a single attack of pyelonephritis. The treatment of pyelonephritis by means of the sulfonamides is now relatively simple, but, as Dr. Crabtree points out, we must be extremely careful in evaluating our results. In addition to the sulfonamides we must overcome anemia, which is fairly common, we must avoid constipation, use the Fowler position for proper drainage, force fluids and give sedatives; we must treat the patient as we did before we had the sulfonamides. The sulfonamide treatment has no bad effect on the babies, and by means of this therapy nearly all patients can be carried to term. As emphasized by Dr. Crabtree, there is apparently no danger that pregnant women will develop a urinary block by crystals if the amount of fluids is not greatly increased. There is now rarely any necessity to employ ureteral catherization or to empty the uterus because of pyelonephritis, but we must remember that the sulfonamides will not cure all patients who have pyelonephritis; hence in an occasional case the pregnancy may have to be terminated. It is difficult to prevent the first attack of pyelonephritis except by removing foci of infection. Much can be done in a prophylactic way by routine microscopic examination of every pregnant woman's urine at every office visit (or oftener when indicated). Once a woman has had pyelonephritis, not only must she be carefully checked for a long time following the first attack but also her urinary tract must be studied before each new pregnancy. Prophylactic therapy with the sulfonamide drugs in successive pregnancies will certainly reduce the incidence of severe recurrences and produce rapid cures, because the patients can be treated early.

DR. BUDD C. CORBUS, Chicago: In November 1927 W. C. Danforth, head of the department of obstetrics at the Evanston Hospital, and I reported our findings in the so-called pyelitis of pregnancy. Our conclusions at that time were as follows: The termination of pregnancy does not cure the urinary infection. These cases should be studied and treated after the pregnancy ends in order to restore adequate urinary drainage if possible. As a pathologic condition of the urinary tract was shown to exist after termination of pregnancy, in all cases studied it seemed reasonable to assume that obstructive pathologic changes may have been present before the pregnancy began. There is no doubt that the pressure of the fetal head and the hormonal influence on the ureter causing dilatation, with lessened

peristaltic action, accompanied by urinary stasis, may be a contributing factor in pyelitis; however, if this was a significant factor more pregnant women would have complicating pyelitis. To me it is the question of the straw breaking the camel's back. I think we can truly consider that pyelitis of pregnancy is a clinical exacerbation of a previous latent chronic urinary tract infection, and in demonstrating this we should not forget the modern conception of the possible pathology of the female bladder neck. We are all aware in urology of the value of the sulfonamide drugs for the nonpregnant woman; we know, however, that they are dangerous and that their administration should be well supervised. The use of drug therapy during an attack of pyelitis of pregnancy by no means replaces complete urologic study after the pregnancy has terminated.

DR. A. J. KOBAK, Chicago: All cases of pyelitis occurring in the obstetric services of Cook County Hospital were studied during a period of twenty-one months and our findings were published. Our material consisted of 143 cases, an incidence of 1.63 per cent. Ninety-five patients had pyelitis ante partum and 48 during the puerperium. It was necessary to interrupt the pregnancy of only 1 patient, and there were no mortalities in the series of cases studied. However, this good fortune was short lived, because subsequent to this report we had three deaths. These patients had more than a simple pyelitis—a pyelonephritis. One woman pregnant for six and one-half months, who had a clinically mild pyelitis, developed pyelonephritis and then eclamptogenic convulsions. The autopsy revealed typical toxemia changes in the liver. The second patient developed pyelonephritis following the birth of a premature baby. The temperature reached a 106 F. level, and the postmortem findings indicated changes in the kidney parenchyma and those of a generalized sepsis, although we never obtained a positive blood culture. The remaining patient four and one-half months pregnant aborted spontaneously, shortly after her admission. She bled sufficiently to warrant a uterine packing. She died after a period of complete urinary suppression and with postmortem evidences of a severe ascending pyelonephritis. All 3 patients had retention of nitrogenous products by blood chemistry analysis. More than one third of the puerperal pyelitis in our reported group had etiologic factors that one frequently observes in patients who develop puerperal sepsis. Thus prolonged labors, difficult forceps deliveries and cesarean sections that were not elective were in this group. Also many of our pyelitis patients had concomitant puerperal sepsis. In view of the anatomic propinquity of the urologic and genital systems, this is not surprising. I wonder if the author can shed any light on this thought that puerperal sepsis and pyelitis may bear a direct mutual relationship.

DR. E. GRANVILLE CRABTREE, Boston: Dr. Kobak, in the reporting of three deaths, brings into prominence the reasons for intensive study that have existed all along and underlie these publications, which is that the handling of these cases in all their complications is not yet simple enough so that perfection can be acquired without the obstetrician becoming an industrious student of this subject.

Aristotle.—Aristotle (384-322 B. C.), the most comprehensive mind of classical antiquity, may be said to have applied to general science the objective method of observation used by Hippocrates in clinical medicine. The other Greek scientists or natural philosophers, such, for instance, as Heraclitus and Parmenides, indulged in vague speculation about the nature of the universe, without bothering to verify their fundamental data. Aristotle obviously made direct observations. He covered an immense field—physics, astronomy, meteorology, psychology, natural history. In biology his work on embryology (De generatione animalium) is full of acute observation; Historia animalium and De partibus animalium furnish a rough, fairly good idea of animal and human anatomy.—Clendening, Logan: Source Book of Medical History, New York, Paul B. Hoeber, Inc., 1942.

CAFFEINE AND "PEPTIC" ULCER

RELATION OF CAFFEINE AND CAFFEINE-CONTAINING BEVERAGES TO THE PATHOGENESIS, DIAGNOSIS AND MANAGEMENT OF "PEPTIC" ULCER

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AND
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In this paper evidence will be presented which strongly indicates that the excessive use of caffeine-containing beverages may contribute to the pathogenesis of "peptic" ulcer in the ulcer-susceptible individual, may aggravate an ulcer already existing and may render the therapeutic management of the condition more difficult. Preliminary studies on ulcer patients suggest the use of a caffeine test meal in the diagnosis of peptic ulcer based on the prolonged secretory curve when the response to caffeine is expressed as the total output of free acid. Additional evidence suggests that a prolonged gastric secretory response to caffeine may provide a method for the detection of those persons who are predisposed to the development of "peptic" ulcer.

LITERATURE

Smoking and the consumption of alcoholic beverages have been interdicted in the management of "peptic" ulcer patients by internists for many years. The consumption of caffeine-containing beverages has not, as a rule, been restricted, except in some instances during the early phase of the management of the active ulcer.

There are several reasons why the relation of caffeine to ulcer and gastric secretion has been a neglected field of investigation. One reason is that caffeine does not stimulate gastric secretion in all species of animals. It does not stimulate gastric secretion in the dog.[1] And it has been shown only recently that caffeine stimulates gastric secretion in the cat.[2] Considerable disagreement is found in the literature concerning the effect of caffeine in man. Various authors [3] have concluded that caffeine does not stimulate gastric secretion in man, whereas others [4] have observed an increased output of acid gastric juice after caffeine administered orally or parenterally. The most recent reviewer of the subject [5] erroneously concluded that caffeine does not stimulate gastric secretion.

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From the Department of Physiology, Northwestern University Medical School.

Read before the Section on Pathology and Physiology at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 14, 1944.

1. Pincussohn, L.: Ueber das Sekretionsförende Prinzip des Kaffees, Ztschr. f. phys. u. diätet. Therap. **11:** 261, 1907. Bickel, A.: Ein Diätschema für die Behandlung der Sekretionsstörungen des Magens, Internat. Beitr. z. Path. u. Therap. d. Ernährungsstör. **1:** 365, 1910. Kestner, O., and Warburg, B.: Die Wirkung der Frühstücksgetränke auf die Verdauungsorgane, Klin. Wchnschr. **2:** 1791 (Sept.) 1923. Roth and Ivy.[2] Wichels, Brink and Lauber.[20]

2. Roth, J. A., and Ivy, A. C.: The Effect of Caffeine on Gastric Secretion in the Dog, Cat and Man, Am. J. Physiol. **141:** 454 (June) 1944.

3. Goldbloom, A.: Experimentelle und klinische Untersuchungen über den Einfluss des Koffeins auf die sekretionische Tätigkeit des Magens, Arch. f. Verdauungskr. **42:** 13 (Feb.) 1928. Ehrman, R., and Dinkin, L.: Magen-Untersuchungsmethoden, Neue Deutsche Klin. **6:** 574, 1930. Oehnell, H., and Berg, H.: Zur Frage über die Ventrikelfunktion nach Verabreichung verschiedenen Orten von Kaffee, Acta med. Scandinav. **76:** 491, 1931. Eichler.[5]

4. Holler, G., and Blöch, J.: Chlorine Metabolism in Disturbances of Stomach Secretion, Arch. f. Verdauungskr. **38:** 351 (Aug.) 1926. Cade, A., and Milhaud, M.: Chimisme gastrique: l'épreuve de la caféine, J. de méd. de Lyon **10:** 523 (Aug.) 1929. Wichels, P.: Coffein als Magensaftlocker, Ztschr. f. klin. Med. **123:** 336, 1933. Katsch and Kalk.[19]

5. Eichler, O.: Kaffee and Coffein—Pharmakologische Wirkungen, Arch. f. exper. Path. u. Pharmakol. **190:** 123, 1938.

The experimental design and technic used in some of the investigations on human subjects were poor in the light of current knowledge. That earlier investigators failed to show conclusively that caffeine has a definite stimulating effect on gastric secretion in man can in part be attributed to (*a*) insufficient exposure of the gastric mucosa to caffeine, (*b*) failure to wait long enough for intramuscular caffeine to produce its effect and (*c*) the fact that the stimulation of secretion by secretagogues in coffee, natural or produced by the roasting process, was not distinguished from the secretion due to caffeine.[6] The peak of the response to the intramuscular administration of caffeine usually does not occur until sixty to seventy minutes after the injection, whereas, when caffeine is given as a test meal, the peak response occurs in from thirty to forty minutes.[2] The prolonged increase in total output of hydrochloric acid in patients with "peptic" ulcer was missed by previous investigators. In order to demonstrate this prolonged response it is necessary to collect gastric secretion for a longer period than one hour and to determine the total output of free acid by multiplying the concentration of acid in the juice by the total volume of gastric contents aspirated (every ten minutes).

PRODUCTION OF GASTRIC ULCER IN CATS

Interest in the possible deleterious effects of excessive amounts of caffeine on the stomach was provoked by a recent report by Judd.[7] Judd observed acute and subacute gastric ulcers in 40 to 50 per cent of cats when they were given caffeine in a beeswax-petrolatum mixture to insure the slow and more prolonged absorption of the drug. We[8] have confirmed the work of Judd and have reported additional observations which may explain in part the pathogenesis of caffeine-induced ulcer.[9]

Direct observation of a mucosal stoma in the cat shows a persistent blushing (hyperemia) after the intravenous administration of caffeine, followed by cyanosis. Microscopic sections, made at the time when the mucosa grossly appeared more reddened, thicker and succulent, showed apparent dilatation and engorgement of veins and venules of the submucosa. However, when the mucosa appeared cyanotic there was pronounced dilatation and engorgement of the mucosal venules. Continuous or repeated stimulation of gastric secretion in the anesthetized cat with histamine for ten to twelve hours produces no apparent change in the gastric mucosa. But, if caffeine (125 mg. intravenously or by direct lavage of the stomach for thirty minutes) is alternated with the histamine (0.3 mg.), large diffuse areas of epithelial desquamation and multiple bleeding erosions and ulcerations of the gastric mucosa are observed in as short a time as five hours. This alteration in the susceptibility of the gastric mucosa to the proteolytic action of gastric juice has been arbitrarily designated and attributed to "cellular toxicity." The latter may involve alteration in cell permeability or the concept of caffeine-histamine synergism. Thus the vascular changes and factor of "cellular toxicity" are implicated in the pathogenesis of caffeine-induced ulcers in cats by increasing the susceptibility of the mucosa to the digestive action of gastric juice.

Comment.—It is realized that these observations on the cat may not be applied directly to man. It is reasonable, however, to estimate how much caffeine might be required in man to produce similar changes in the gastric mucosa. Since 2 grains (125 mg.) of caffeine in combination with "histaminergic" stimulation of gastric secretion (0.3 mg. of histamine dihydrochloride, alternately) was capable of producting acute ulcers in a 5 pound (2.3 Kg.) cat, 60 grains (7.8 Gm.) of caffeine would be required in a 150 pound (68 Kg.) man on the basis of body weight. However, body weight comparisons are not always reliable. For example, a dose of 0.5 or 1.0 mg. of histamine stimulates gastric secretion in man and dog; a dose of 62.5 to 125 mg. of caffeine stimulates gastric secretion in the cat, and 80 to 250 mg. in man. It is reasonable to hypothecate that the daily consumption of 20 or 30 grains of caffeine over a long time (equivalent to ten to fifteen cups of coffee) may contribute to the development of "peptic" ulcers in ulcer-susceptible individuals. We have not had an opportunity to make observations on a patient with a gastric fistula or during gastroscopy.

THE GASTRIC SECRETORY RESPONSE TO CAFFEINE IN MAN: NORMAL SUBJECTS AND "PEPTIC" ULCER PATIENTS

The gastric secretory response to a "caffeine test meal" has been determined in 50 asymptomatic medical students and nurses and in 36 patients under management for "peptic" ulcer.

The ordinary gastric analysis is designed to answer one or two questions: (*a*) Does the stomach secrete free acid in response to a meal (Ewald or some modification)? (*b*) If not, is the stomach capable of secreting free acid in response to a more potent stimulus (histamine)? Since the "caffeine test meal" as used by us consists of more than the ordinary gastric analysis, and since it may prove to be of diagnostic or prognostic value, we shall briefly describe it:

The Caffeine Test Meal.—After an overnight fast, the usual precautions regarding expectoration of saliva, the avoidance of retching by placing the tube between the teeth and the cheek, and completeness of evacuation of the stomach at each period are followed. After removal of the residuum, a baseline from which stimulation can be measured is obtained by emptying the stomach every ten minutes for a control period of thirty minutes. The total volume recovered at each ten minute aspiration is measured and a sample (10 cc.) titrated for free and total acid, expressing the latter in terms of the total volume aspirated (volume times concentration).

Then, 200 cc. of warm water containing 0.5 Gm. (7½ grains) of caffeine with sodium benzoate is introduced into the stomach through the tube. The resulting solution is slightly alkaline, having a p_H of about 8.0. A "block" procedure was then followed for the analysis: for the next two ten minute intervals, 10 cc. samples were removed for analysis. The purpose in removing these samples was to detect the first rise in acid concentration and thus the latent period of stimulation. To simplify the procedure for clinical use, the aspiration of these two samples may be omitted. Thirty minutes after introducing the test meal, the residuum of the latter and whatever gastric secretion has accumulated is removed completely. The stomach is emptied at ten minute intervals thereafter for an additional ninety minutes or until the secretory response has subsided and the "basal" level once again is obtained. The duration of the test is thus two hours and thirty-five minutes divided as follows: removal of residuum, thirty minute "basal" control period, five minute period required to introduce the test meal,

6. Bickel, A., and Van Eweyk, C.: Zur Kenntnis der die Magensaftbildung und die Magen-Darmbewegung anregenden Substanzen im Kaffee-Infus, Ztschr. f. d. ges. exper. Med. **54**: 75, 1927. Oehnell and Berg.[3]

7. Judd, E. S.: Experimental Production of Peptic Ulcers with Caffeine, Bull. Am. Coll. Surg. **28**: 46 (Aug.) 1943.

8. Roth, J. A., and Ivy, A. C.: The Experimental Production of Acute and Subacute Gastric Ulcers in Cats by the Intramuscular Injection of Caffeine in Beeswax, Gastroenterology **2**: 274 (April) 1944.

9. Roth, J. A., and Ivy, A. C.: The Pathogenesis of Caffeine-Induced Ulcers, Gastroenterology, to be published.

thirty minute period of exposure of the gastric mucosa, and a ninety minute period of aspirations every ten minutes after removal of the test meal.

Titrations and Calculations.—Titrate the 10 cc. samples of gastric juice with thirty-sixth normal sodium hydroxide (may be made by the addition of 20 Gm. of sodium hydroxide to 18 liters of water), using Toepfer's reagent and phenolphthalein as the indicators for free and total acid respectively. As 1 cc. of thirty-sixth normal sodium hydroxide is equivalent to 1 mg. of hydrochloric acid, the buret readings can be converted directly into milligrams of hydrochloric acid. To obtain the total output of free and total acid, the buret readings are divided by 10 to give the number of milligrams of hydrochloric acid per cubic centimeter of gastric juice and multiplied by the volume aspirated. The accuracy of the test thus depends on the ability of the technician to empty the stomach of its contents completely, which is relatively easy.

Buret reading = mg. HCl/10 cc. gastric juice (sample)

$$\text{Total output of acid} = \frac{\text{buret reading}}{10} \times \text{total volume aspirated}$$

The Response of Special Cases.—The data in table 1 are presented to illustrate the individual variations and range in response to a caffeine test meal in the various groups of normal subjects and ulcer patients. It is to be noted that where the acid output for the second hour remains high this reflects the prolonged secretory curve in which a high level of acid is maintained (charts 3, 4 and 5). Certain of the cases have been selected to point out particular features in the use of the caffeine test meal for the diagnosis of ulcer. Patient H. P., partially obstructed at the time the test was performed, showed an absence of free acid in the "basal" control period but maintained a stimulation of gastric secretion at a relatively low level throughout the test. Not all patients with a prepyloric ulcer show a tendency for the secretory response to return to the "basal" level toward the end of the two hours as demonstrated in the case of L. F. The highest magnitude of stimulation in this series of ulcer patients was obtained in W. M.; three weeks after the test was performed the patient developed an acute perforation. Patient J. J., with the diagnosis of catatonic schizophrenia, was admitted to the hospital after a

TABLE 1.—*The Effect of Caffeine on Gastric Secretion in Normal Subjects and Ulcer Patients*

	Control: "Basal" Secretion			Caffeine Test Meal: 250 Mg. Caffeine in 200 Cc. Water						
	Total Juice Secreted in ½ Hour			Total Juice Secreted in 1st Hour			Total Juice Secreted in 2d Hour			
Subject	Volume, Cc.	Free Acid, Mg. HCl	Total Acid, Mg. HCl	Volume, Cc.	Free Acid, Mg. HCl	Total Acid, Mg. HCl	Volume, Cc.	Free Acid, Mg. HCl	Total Acid, Mg. HCl	Comment
J. R.*	22	0	6	69	185	214	...	...	...	Normal subject; abrupt, transient response
G. D.*	15	0	6	95	162	193	...	...	...	Normal subject; abrupt, transient response
P. W.*	58	5	35	128	57	96	...	...	...	Normal subject; abrupt, transient response
J. W.*	25	0	14	62	54	74	...	...	...	Normal subject; low flat curve
J. K.*	28	0	11	94	95	148	...	...	...	Normal subject; low flat curve
J. I.	95	69	111	200	425	507	122	361	419	"Normal" subject; developed symptoms 6 months later
A. U.	35	59	69	130	265	300	99	339	376	"Normal" subject; developed symptoms and x-ray evidence 3 months later
G. J.	64	21	39	115	219	308	80	104	173	Prepyloric ulcer; symptoms 19 years; pyloroplasty
H. P.	48	0	27	287	86	166	164	72	127	Prepyloric ulcer; symptoms 9 years; obstructed
L. F.	62	87	115	180	393	451	120	257	313	Prepyloric ulcer; symptoms 6 years; severe hematemesis, coffee distress
W. M.	61	198	227	282	923	1,045	315	1,279	1,413	Duodenal ulcer; symptoms 9 months; severe hematemesis; perforation 3 weeks after test; coffee distress
J. J.	74	55	76	102	192	239	229	340	417	Duodenal ulcer suspected from caffeine test meal; no symptoms, x-ray negative; severe hematemesis; red blood cells 2,000,000
C. T.	51	76	86	72	156	181	88	226	262	Duodenal ulcer; symptoms 9 years; hematemesis four times; rapid emptying; concentration remains elevated; coffee distress

* No figures appear for the second hour, since the response had returned to the "basal" level within sixty minutes.

Response of Normal or Asymptomatic Subjects.—Three types of response were obtained in the normal or asymptomatic subjects when the data were plotted as a "total output of acid" curve. Thirty-seven, or 75 per cent, showed an abrupt, transient stimulation with a peak followed by a return to the control level within sixty to seventy minutes (chart 1). In 15 per cent, a low flat curve was obtained which returned to the control level in seventy to eighty minutes (chart 2).

The remaining 5 subjects, or 10 per cent, showed a prolonged secretory response (chart 3). It is noteworthy that 3 of these 5 subjects have since developed epigastric distress, simulating ulcer, and in one a prepyloric ulcer has been found by x-ray (table 1).

The Response of Ulcer Patients.—Of the 36 patients studied, 30 had proved duodenal ulcer and 6 gastric ulcer.[10]

All of these patients, with the exception of 1, have consistently shown a prolonged response to the caffeine test meal (charts 4 and 5). Though the cases are relatively few, there is a greater tendency for the gastric ulcer patient to return to the control level toward the end of two hours than the duodenal ulcer patient.

severe attack of hematemesis with a red blood cell count of 2,000,000. The anamnesis and x-ray examination of the stomach and duodenum gave no indication of peptic ulcer, but the prolonged secretory curve in response to caffeine confirms the most probable cause of such severe hemorrhage in a man aged 24 in whom no cause could otherwise be demonstrated. This instance illustrates the most useful application of the caffeine test meal; i. e., where other laboratory aids fail to confirm the history or where a silent ulcer is revealed. The low volume of gastric juice recovered during the test on patient C. T. indicates rapid emptying through the pylorus, but the concentration of acid (milligrams of hydrochloric acid per cubic centimeter) remained elevated throughout the test. This has been interpreted as consistent with the ulcer response since normal subjects show a return to the "basal" concentration as well as to the "basal" total output of acid, although the differences between normal and ulcer concentration curves (clinical units) are not as great as in total output curves (chart 6). Only 1 of the group of 36 ulcer patients studied showed such rapid emptying of the stomach as to present the foregoing picture.

Comparison of Responses of Ulcer Patients to Alcohol and to Caffeine.—Rehfuss, according to Bockus,[11] was the first to observe the tendency for patients with duodenal ulcer to manifest a prolonged or "terminal" response to a test meal. This has been reported by

10. The majority of the ulcer patients used in this study were provided by Drs. Kipnis, Baker, Carroll and Trauba at the Hines Veterans' Hospital.

11. Bockus, H. L.: Gastroenterology, Philadelphia, W. B. Saunders Company, 1943, vol. 1, p. 407.

others.[12] In their studies the concentration of acid in clinical units was followed. In our work, as in laboratory animals, we have calculated and used the total output of acid secreted. We believe this to be preferable because the total output of acid is a truer index of the secretory response than the concentration of acid. To

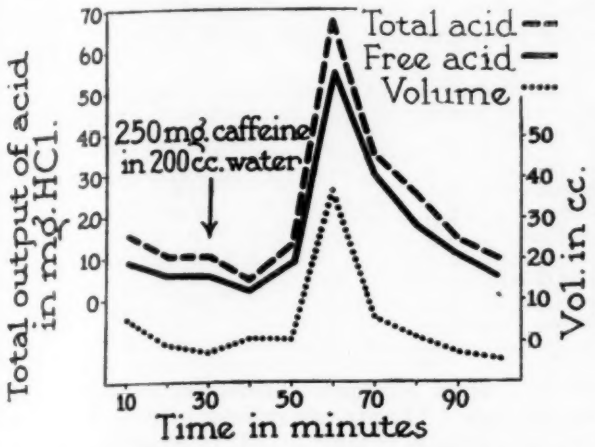

Chart 1.—Composite curves on 37 normal subjects (75 per cent) showing abrupt transient stimulation of gastric secretion in response to caffeine test meal.

do this with the intact stomach a "block" procedure (vide supra) is required, since it cannot be done by the "sampling" technic.

Because the alcohol test meal is frequently used and because alcohol is frequently interdicted in patients with "peptic" ulcer, we have compared alcohol with caffeine as gastric stimulants. Ten of the "peptic" ulcer patients were given the alcohol (200 cc., 5 per cent) and caffeine test meals. Twenty-five normal asymptomatic subjects were similarly studied. In each case the "block" procedure as described was used. The composite "total output of acid" curves of normal subjects and "peptic" ulcer patients are shown in chart 7.

In both groups an abrupt transient stimulation with a peak and return to the control level within sixty to seventy minutes occurred in response to alcohol.

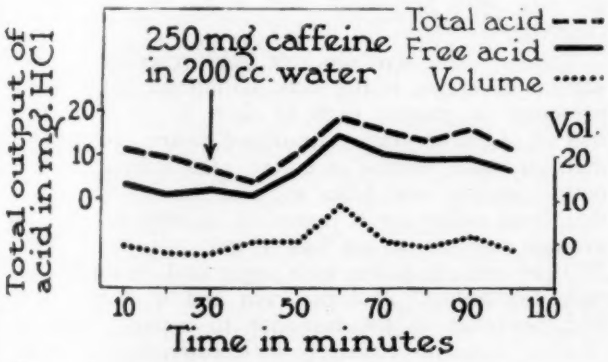

Chart 2.—Composite curves on 8 normal subjects (15 per cent) showing low flat secretory curve in response to caffeine test meal.

Although the average magnitude of the response to alcohol is higher in the duodenal ulcer patients, the shape of the curves and the duration of the responses are the same. Since the magnitude of the response to alcohol in normal subjects and "peptic" ulcer patients overlap so decidedly in the two groups, the differences are not statistically significant and are of little differential value. This was not true of the caffeine test meal except in 10 per cent of asymptomatic subjects who apparently have a predisposition to "peptic" ulcer.

Comment.—Although sufficient evidence has been presented to show that the stomach of the "peptic" ulcer patient, especially the duodenal ulcer patient, manifests a more prolonged response to caffeine than that of the "normal" subject, certain questions are still open. A sufficient number of duodenal ulcer patients have not been studied to ascertain if all will show a prolonged response. A sufficient number of gastric ulcer patients have not been studied to ascertain if they as a rule respond differently from duodenal ulcer patients. Whether the response of duodenal ulcer patients to the caffeine test meal returns to the normal type during a remission has not been determined.

Our results suggest that it would be valuable to determine with what degree of accuracy predisposition to "peptic" ulcer may be predicted by the response to the caffeine test meal. In this connection one should recall the observations of Todd[13] on medical students.

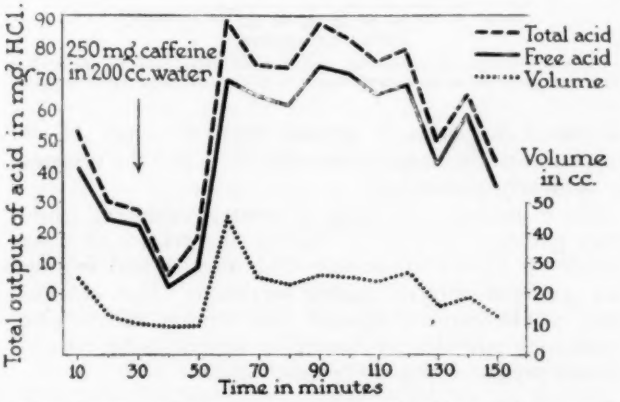

Chart 3.—Composite curves on 5 "normal" subjects (10 per cent) showing prolonged response at a high level of acidity like the ulcer patient.

He found (*a*) that a small group of students responded to anxiety by manifesting a hypermotile and hypertonic stomach and (*b*) that it was only in this group that duodenal ulcer developed sometime during the medical course.

The practical points which we believe our data establish are that caffeine causes a prolonged response in duodenal ulcer patients, and it would seem to be indicated that this fact should be considered in the management of such patients.

CAFFEINE ACTS SYNERGISTICALLY WITH HISTAMINE OR ALCOHOL

It has been reported elsewhere that caffeine acts synergistically with histamine or alcohol.[14] This matter was studied for practical as well as for academic reasons.

First, why does caffeine cause a prolonged gastric secretory response in patients with "peptic" ulcer? There is strong presumptive evidence showing that the phase of gastric secretion which cannot be inhibited by atropine is due to the production of histamine.[15] If

12. Bockus, H. L.; Glassmire, C., and Bank, J.: Fractional Gastric Analysis in 200 Cases of Duodenal Ulcer, Am. J. Surg. **12**: 6 (April) 1931.

13. Todd, T. W.: Behavior Patterns of the Alimentary Tract, Tr. Am. Gastroenterol. A. **32**: 487, 1930. Schiffrin, M. J., and Ivy, A. C.: Physiology of Gastric Secretion, Particularly as Related to the Peptic Ulcer Problem, Arch. Surg. **44**: 399 (March) 1942.

14. Roth, J. A., and Ivy, A. C.: The Synergistic Effect of Caffeine on Histamine in Relation to Gastric Secretion, Am. J. Physiol., to be published.

15. Ivy, A. C.: The Mechanisms of Gastric Secretion, Surgery **10**: 861 (Dec.) 1941.

the ulcer patient produces histamine and since histamine and caffeine act synergistically, this would explain the prolonged response of the ulcer patient to caffeine. It has been shown [14] that when the two drugs are given together to a nonulcer subject the magnitude of the

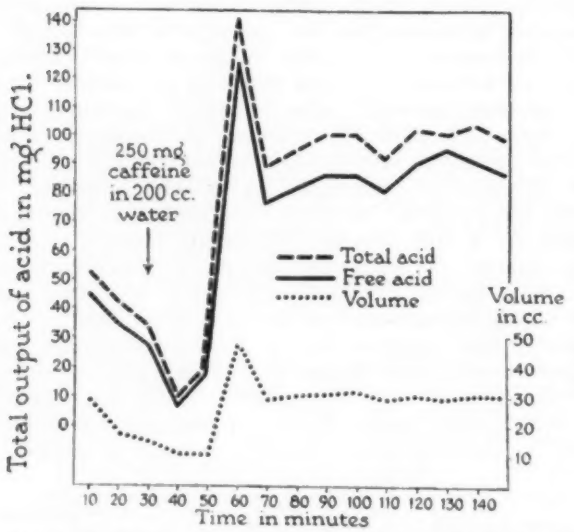

Chart 4.—Composite curves on 30 duodenal ulcer patients showing a prolonged stimulation at a high level of acidity in response to caffeine.

combined response is greater than the sum of the responses to the drugs given separately and the response is definitely prolonged.

Since alcohol, according to strong evidence, stimulates gastric secretion by causing the release of histamine,[16] it is not surprising that alcohol and caffeine act synergistically on gastric secretion. This observation would caution against the mixing of caffeine-containing and alcohol-containing beverages by persons with a predisposition to "peptic" ulcer.

RESPONSE TO CAFFEINE-CONTAINING AND SUBSTITUTE BEVERAGES

After studying the gastric secretory response to pure caffeine in normal subjects and ulcer patients, our attention was directed to the practical problem of the

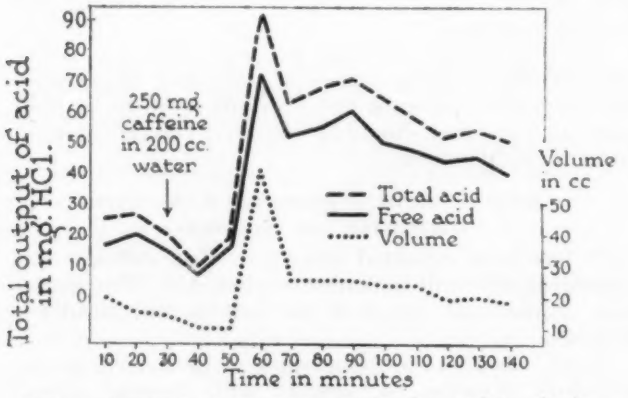

Chart 5.—Composite curves on 6 gastric ulcer patients showing a tendency to return to "basal" level during the second hour period.

response to various caffeine-containing beverages and substitute beverages.

Method.—The same procedure as outlined for the caffeine test meal was used in these studies. The beverages selected for study included coffee, coffee with sugar (10 Gm.) and cream (30 cc., 18 per cent), "Sanka," "Postum," "Coca Cola" and tea. An attempt was made to make the preparations of the beverages uniform by using a constant weight of the dry product per unit volume and by being consistent in the time of extraction. Each beverage was prepared according to the directions on the label of the product. The volume of the beverages used for test meals in the studies was

TABLE 2.—*Average Caffeine Content of Various Beverages*

Beverage [17]	Approximate Caffeine Content	
	Mg./Cup or Bottle	Grains/Cup or Bottle
Coffee	100-120	1½-2
Pepsi Cola	77	1⅛
Spur	57	⅞
Coca Cola	33	½
Tea	17-33	¼-½
Sanka	8-17	⅛-¼

300 cc., which is approximately the volume of two average cups. The average caffeine content of various beverages appears in table 2.[17] It is apparent from this table that 2 cups of coffee contain approximately the same amount of caffeine as used in the caffeine test meal (250 mg. caffeine base). As the color of the beverage interfered with colorimetric titrations, it was necessary to do electrometric titrations, using as an end point

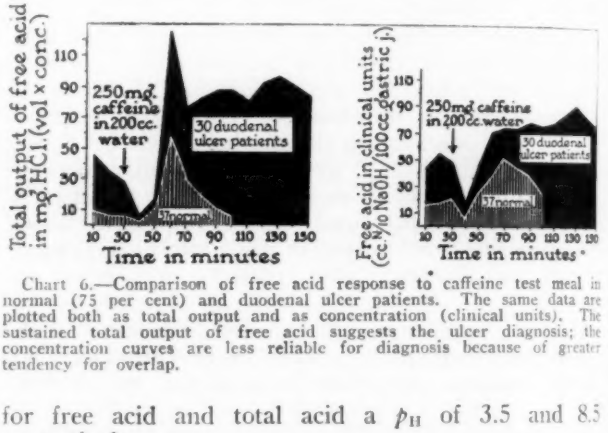
Total output of free acid in mg. HCl (vol x conc.)
250 mg. caffeine in 200 cc. water
30 duodenal ulcer patients
57 normal
Time in minutes
Free acid in clinical units (cc. % NaOH/100 cc. gastric juice)
250 mg. caffeine in 200 cc. water
30 duodenal ulcer patients
57 normal
Time in minutes

Chart 6.—Comparison of free acid response to caffeine test meal in normal (75 per cent) and duodenal ulcer patients. The same data are plotted both as total output and as concentration (clinical units). The sustained total output of free acid suggests the ulcer diagnosis; the concentration curves are less reliable for diagnosis because of greater tendency for overlap.

for free acid and total acid a p_H of 3.5 and 8.5 respectively.

Results.—The average free acid response to these various beverages in the same 10 normal individuals is presented in graphic form in chart 8. It is apparent that all of the beverages stimulated gastric secretion less than an equal volume of coffee. Comparing the total output of free acid from each of the beverages with that from coffee for a period of seventy minutes, the average response to tea was 60 per cent, to "Postum" 59.3 per cent, to coffee with sugar and cream 59.7 per cent, to "Sanka" 75.3 per cent and to "Coca Cola" 89.5 per cent of the response to coffee. Although "Sanka" contains relatively little caffeine, it provokes

16. Dragstedt, C. A.; Gray, J. S.; Lawton, A. H., and Ramirez de Arellano, M.: Does Alcohol Stimulate Gastric Secretion by Liberating Histamine? Proc. Soc. Exper. Biol. & Med. **43**: 26 (Jan.) 1940.

17. References cited in table 2:

Coffee:
Sollmann, T.: A Manual of Pharmacology, Philadelphia, W. B. Saunders Company, 1926, p. 282.
Bethea, O. W.: Caffeine Beverages, Internat. M. Digest **27**: 46 (July) 1935.

Pepsi Cola, Spur and Coca Cola:
New Hampshire Health News, July 1941, vol. 19.

Tea:
Aubert, H.: Ueber den Coffeingehalt des Kaffeegetränkes und über die Wirkungen des Coffeins, Arch. f. d. ges. Physiol. **5**: 589, 1872.

Sanka:
Examination of Three Caffeine-Reduced (So-Called Decaffeinated) Coffees, report of the Chemical Laboratory, J. A. M. A. **91**: 880 (Sept. 22) 1928.

considerable stimulation of gastric secretion, presumably because of its content of other secretagogues ("Sanka," because of its secretagogue rather than caffeine content, stimulates gastric secretion in the dog; caffeine does not). We have confirmed the report that a so-called decaffeinated coffee preparation stimulated gastric secretion in patients with hyperchlorhydria and "peptic" ulcer about the same as coffee.[18]

In chart 9 appears the total output curves for free acid in response to coffee (300 cc.) in both normal subjects[19] and duodenal ulcer patients.[20] The ulcer patients have consistently shown a prolonged secretory response to the coffee test meal, maintaining a high level of acidity at the termination of the test. However, in the few instances in which it was tried a coffee substitute which contains no caffeine did not provoke a hypercontinuous secretion of gastric juice.

Comment.—It is believed that the foregoing observations warrant the following recommendations in the management of the "peptic" ulcer patient: The consumption of caffeine-containing beverages should be restricted to a minimum in view of the magnitude and duration of the gastric secretory response. If small amounts are allowed, they should be taken with cream and sugar. In our series of 36 ulcer patients, 70 per cent reported that they had observed that coffee aggravated their symptomatic distress.

It is well known that much sound clinical judgment and persuasion must be exercised in the management of the patient with "peptic" ulcer. It should be clear that, because a substance stimulates gastric secretion, this in itself is not a sound reason for its interdiction. Otherwise we should interdict protein food which serves an important role in the therapeutic rationale of frequent feedings with milk and cream.

Since caffeine and caffeine-containing beverages do not provide a "buffering effect" but provoke a prolonged secretion of acid in ulcer patients, and since caffeine produces vascular and "cellular" changes which apparently render the mucosa susceptible to erosion, such beverages should be avoided by the ulcer patient. This is particularly true of their excessive use. It is realized that the psychologic hardship of total abstinence is sometimes more aggravating to the ulcer patient than the pharmacodynamic effects of a contraindicated substance. In such instances a single cup of coffee with sugar and milk or cream with the meal could be allowed. Or one might substitute a beverage of lower caffeine content, such as tea or some coffee substitute, some roasted cereal product low in those secretagogues produced by roasting.

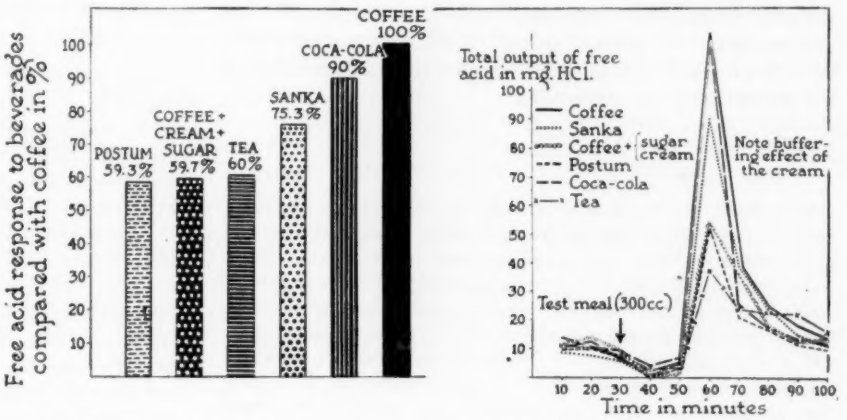

Chart 8.—Composite free acid curves in response to related beverages in 10 normal subjects. The columns show the free acid response to the beverages when compared to the coffee response in percentage.

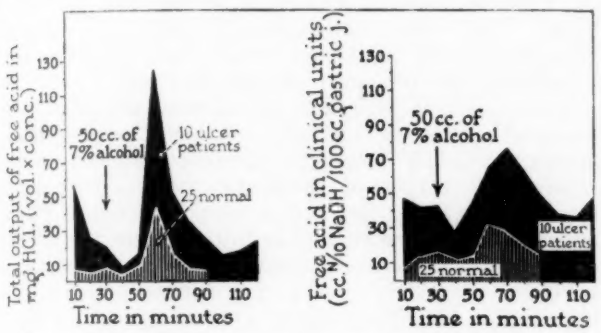
Total output of free acid in mg. HCl. (vol. x conc.)
50cc. of 7% alcohol
10 ulcer patients
25 normal
Time in minutes
Free acid in clinical units (cc. % NaOH/100 cc. gastric j.)
50cc. of 7% alcohol
10 ulcer patients
25 normal
Time in minutes

Chart 7.—Comparison of free acid response to alcohol test meal in normal and ulcer patients. The similarity in the shape of the curves and the overlap in magnitude of response limits the use of the alcohol test meal in diagnosis.

CONCLUSIONS

1. Caffeine in relatively large doses causes acute and subacute ulceration of the gastric mucosa in cats.
2. Caffeine (80 to 250 mg.) stimulates gastric secretion in man and the cat but not in the dog.
3. Caffeine acts synergistically with histamine or alcohol in stimulation of gastric secretion in man and the cat.
4. Caffeine-containing beverages stimulate gastric secretion in man. Coffee substitutes produced by roasting cereal contain secretagogues which stimulate gastric secretion in man. Coffee stimulates gastric secretion because of its caffeine content and because of other secretagogues (natural, roast products or irritant volatile oils).
5. Caffeine and caffeine-containing beverages provoke a prolonged increase in the total output of acid by the stomach in patients with "peptic" ulcer.

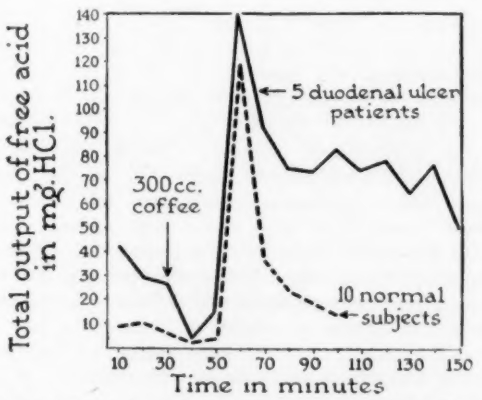

Chart 9.—Comparison of the free acid response to a coffee test meal in normal subjects and duodenal ulcer patients. Note the sustained stimulation in the ulcer patients in contrast to the abrupt, transient response in normal subjects.

18. Bernay, P., and Faure, G.: Café décaféine et tabac denicotinisé en diététique gastrique, Arch. d. mal. de l'app. digestif. **27**: 865 (Oct.) 1937.
19. Katsch, G., and Kalk, H.: Zum Ausbau der kinetischen Methode für die Untersuchung des Magenchemismus, Klin. Wchnschr. **4**: 2190 (Nov.) 1925.
20. Wichels, P.; Brink, J., and Lauber, H.: Beiträge zur Pathogenese der Gastritis. Leberschaden und Magenkrankheit, Ztschr. f. klin. Med. **123**: 325 (Oct.) 1933.

6. Five of a group of 50 "normal" or asymptomatic human subjects responded to the caffeine test meal like an ulcer patient. Three of the 5 have subsequently developed the ulcer type of distress, and 1 of these has developed an ulcer as demonstrated by x-ray.

7. The evidence indicates that the excessive use of caffeine-containing beverages may contribute to the pathogenesis of "peptic" ulcer in the ulcer susceptible person and will render the therapeutic management of the condition more difficult.

ABSTRACT OF DISCUSSION

DR. A. F. R. ANDRESEN, Brooklyn: After experimenting with coffee in ulcer patients, I began thirty years ago to forbid its use in ulcer diets and have continued to do so ever since. This in contradistinction to smoking, which I have found is rarely harmful and then probably explainable on an allergic basis. The demonstration that caffeine given to human beings will produce an acid curve of continued secretion in a series of fractional removals of gastric contents thereafter is an indication of irritation. The similar curve, a continued or rising secretion for a period of two hours or more following injection of histamine instead of the normal, physiologic rise and fall after one hour, has been demonstrated in most ulcer cases and we have always explained it on the basis of gastric irritation produced by the presence of the ulcer. Histamine appears to be a physiologic stimulant to gastric secretion, Ivy having demonstrated its identity with gastric hormone, and is therefore the best stimulant to secretion that can be used in gastric analysis. The combination of an irritant such as caffeine with the histamine would not seem advisable as a routine procedure, as the response would not be a good test of the patient's usual secretory habits. The suggestion that human peptic ulcers may be caused by the taking of caffeine does not seem to be justified, although sudden excessive consumption of caffeine by patients subject to the development of ulcers might conceivably be the irritant which started an attack. The diffuse areas of superficial erosion or sloughing seen in the experiments on the cats, evidences of a poisoning, do not at all resemble discrete human peptic ulcers. Prevention of ulcers by abstinence from caffeine is not borne out clinically. If other factors tending to produce an ulcer have not been eliminated, abstinence from caffeine has not prevented their recurrence and I have found that patients whose focal infections have been thoroughly eradicated can drink coffee with impunity.

DR. THEODORE J. CURPHEY, Garden City, N. Y.: I should like to ask Dr. Ivy whether he has used this test in the equivocal case, roentgenologically speaking; whether it has been possible to establish the presence of ulcer or rule out the presence of ulcer on the basis of an evasive or equivocal x-ray finding.

DR. HEINRICH NECHELES, Chicago: Caffeine has been used for stomach tests a long time in Europe. I wonder why it has not found wider application. Starkenstein has shown why ulcer patients should drink their coffee with cream or milk, because with the latter substances the toxicity of caffeine is actually lowered. Apparently a slower absorbed and less toxic compound is formed between lipoid and caffeine. Rats injected with a minimal toxic dose of caffeine or black coffee died in a short time. They lived when the same amount of caffeine or of black coffee was mixed with milk or with cream.

DR. A. C. IVY, Chicago: In regard to the equivocal case, so far we have had experience with only 1 patient who had hematemesis for some obscure reason. No niche or disturbance could be found on x-ray examination. The patient gave the typical caffeine curve of duodenal ulcer. I have forgotten whether or not an operation was done; but we thought that the hemorrhage was due to bleeding from superficial lesions of the gastric mucosa. In regard to the literature cited by Dr. Necheles, that literature is covered in our complete manuscript and could not be reviewed in the time allowed.

THE EFFECT OF PENICILLIN ON RHEUMATOID ARTHRITIS

MAJOR EDWARD W. BOLAND
CAPTAIN NATHAN E. HEADLEY
AND
LIEUTENANT COLONEL PHILIP S. HENCH
MEDICAL CORPS, ARMY OF THE UNITED STATES

The cause of rheumatoid (atrophic) arthritis is unknown. Of the many impressions regarding its cause, the microbic hypothesis is still the most widely accepted and, of the many different bacteria which have been incriminated, hemolytic streptococci have been, since 1929, most under suspicion.[1]

Hemolytic streptococci from time to time have been recovered from the synovial fluid and blood, from foci of infection and occasionally from synovial membrane, bone and lymph nodes of patients with rheumatoid arthritis. The blood of the majority of patients who have this disease contains antibodies against hemolytic streptococci; that is, agglutinins, generally in high titer and precipitins for the C substance of hemolytic streptococci. Although the concentration of antistreptolysins and antifibrinolysins in the blood is not increased, except in some early or acute cases, the skin of patients with rheumatoid arthritis often is found to be hypersensitive to extracts of hemolytic streptococci.

Such is the direct and indirect evidence on which the argument against hemolytic streptococci has been based. But since many patients with unmistakable rheumatoid arthritis do not present such evidence, the hypothesis has remained presumptive only.

Ever since it was announced that penicillin was extremely effective against a variety of infectious agents, including hemolytic streptococci, many physicians and a host of rheumatic patients have been hopefully awaiting news that penicillin might prove effective against rheumatoid arthritis. True, the sulfonamides, also effective against hemolytic streptococci, have proved useless against this disease.[2] But it was hoped that penicillin might somehow prove to have power superior to sulfonamides against hemolytic streptococci or, if hemolytic streptococci were not the cause of rheumatoid arthritis, perhaps penicillin might kill the "undiscovered germ" of the disease. Hence, even though we never had accepted hemolytic streptococci as the cause,[1] we were pleased when the War Department and the Surgeon General's Office authorized the staff of the Rheumatism Center of the Army, at the Army and Navy General Hospital,[3] to give penicillin a clinical trial in rheumatoid arthritis.

PLAN OF INVESTIGATION

Two chief policies governed our investigation:

Policy Regarding Selection of Cases.—The only cases chosen for trial of treatment with penicillin were those in which the disease had advanced far enough to be diagnostically unmistakable but not far enough to have produced irreversible changes (destruction of cartilage

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Lieutenant Colonel Hench is on leave of absence from the Division of Medicine, Mayo Clinic, Rochester, Minn.

From the Rheumatism Center of the United States Army, Army and Navy General Hospital, Hot Springs, Ark.

1. Hench, P. S.: Is Rheumatoid (Atrophic) Arthritis a Disease of Microbic Origin? A Summary of the Arguments For and Against the Infectious Theory, in Gordon, R. G.: A Survey of Chronic Rheumatic Diseases, Contributed by Contemporary Authorities in Commemoration of the Bicentenary of the Royal National Hospital for Rheumatic Diseases, Bath, 1738-1938, New York, Oxford University Press, 1938, pp. 35-62.

2. Coggeshall, H. C., and Bauer, Walter: The Treatment of Gonorrheal and Rheumatoid Arthritis with Sulfanilamide, New England J. Med. **220**: 85-103 (Jan. 19) 1939.

3. Hench, P. S., and Boland, E. W.: Unpublished data.

and subchondral bone, notable flexion deformities), the presence of which might have made difficult a clearcut evaluation of results.

Policy Regarding Dosage.—We decided to give penicillin long enough and in large enough doses so that, were our results negative, it could not well be said that our patients had not received sufficient amounts of the material.

PATIENTS TREATED

Ten patients have been treated intensively (table 1). All were male soldiers recently on active duty. Their ages were from 23 to 45 (average 30) years.

Duration of Illness.—Eight of the patients never had had the disease prior to active duty. Two of the patients had had the disease mildly in civilian life. One of these 2 (patient 7) had had three interrupted periods of mild arthritis between 1930 and 1934, then none until 1943; the other (patient 10) had had mild periodic sacroiliac backache since 1938, but the peripheral joints had been affected only in the past thirteen months. Excluding the disease from which these 2 patients had suffered before they entered military service, the 10 patients had been ill from two to eighteen months, an average of 7.4 months. Thus, their disease was in a fairly early stage.

Symptoms.—The symptoms were characteristic of rheumatoid arthritis: aching, soreness, stiffness and "jelling" of joints and muscles; weakness, fatigue, malaise, loss of appetite, some loss of weight and hyperhidrosis of the extremities. Five of the patients walked with a limp; 1 was temporarily bedridden. Before they had come to this hospital, the patients had been treated with salicylates, rest, vitamins, sulfonamides (no effect) and the removal of tonsils (2 cases) and teeth.

Examination of Joints.—Despite its relatively short duration, the disease had been decidedly progressive, such that in every case several or many joints were involved. Extension of the disease, therefore, was graded 2 and 3 on a scale in which 1 would indicate the least and 4 the greatest extension (table 1). The joints presented the classic picture of advancing rheumatoid arthritis: symmetrical, fusiform swelling of the fingers; thickened, tender metatarsals; swollen toes, ankles, wrists, knees and so forth. In 6 cases definite effusion was present in the knees. There were early slight flexion deformities of the knees in 4 cases and of the elbows in 2 cases. Several patients exhibited mild but definite muscular atrophy. Therefore the activity of the disease was graded 2 to 2 plus (table 1).

Roentgenograms.—In no case were there as yet any notable roentgenographic alterations in the joints, such as definite thinning of joint spaces or irregularities in bony contour. Present in some joints were increases in periarticular shadows and evidence of slight atrophy of bone.

Laboratory Data.—Sedimentation rates were determined by the Wintrobe method (normal values 0 to 9 mm. per hour). Rates were increased in every case (table 1). Of the 10 patients, 4 had slight secondary anemia (hemoglobin 11 to 12.5 Gm. per hundred cubic centimeters) and 1 had moderate anemia (hemoglobin 9.5 Gm. per hundred cubic centimeters). Blood cultures, made in every case, were negative. Cultures and smears for bacteria in the synovial fluid were made in 6 of the 10 cases and in all results were negative. Agglutinations for brucellosis and serologic tests for syphilis gave negative results in the 10 cases. In 4 of the 10 cases leukocyte counts were made of the synovial fluid (table 2).

TABLE 1.—*Effect of Penicillin on Rheumatoid Arthritis*

Case	Age, Years	Duration of Current Symptoms, Months	Activity of Disease*	Extension of Disease	Penicillin: Daily Dosage in Oxford Units (Intramuscular) and Days Given	Penicillin: Total Dose	Penicillin: Days Treated	Clinical Results: Objective	Clinical Results: Subjective	Sedimentation Rate, Mm. per Hour: Before Treatment	Sedimentation Rate, Mm. per Hour: After Treatment
1	39	8	2+	3	320,000 for 5 days, 160,000 for 10 days.....	3,200,000	15	No change	No change	45	43
2	45	18	2	3	320,000 for 5 days, 160,000 for 10 days (25,000 intra-articular twice)	3,250,000	15	No change	No change	31	28
3	28	6	2	2	160,000 for 20 days.....	3,200,000	20	No change	No change	21	31
4	31	9	2	3	160,000 for 20 days.....	3,200,000	20	No change	No change	39	41
5	28	4	2	2+	240,000 for 1 day, 120,000 for 13 days.....	1,800,000	14	No change	No change	35	30
6	34	5	2	2+	240,000 for 1 day, 120,000 for 13 days.....	1,800,000	14	No change	Slightly improved	53	50
7	31	6	2	2	240,000 for 1 day, 120,000 for 13 days.....	1,800,000	14	No change	No change	45	43
8	24	3	2	2	240,000 for 1 day, 120,000 for 13 days.....	1,800,000	14	Improved	Improved	36	43
9	23	2	2	2	240,000 for 1 day, 120,000 for 13 days.....	1,800,000	14	No change	Worse	35	25
10	23	13	2+	2+	240,000 for 1 day, 120,000 for 13 days.....	1,800,000	14	No change	No change	55	63

* Grade 1 would indicate the least, and grade 4 the greatest, activity.

TABLE 2.—*Leukocytes per Cubic Millimeter of Synovial Fluid*

Case	Before Treatment	After Treatment
5.....	38,000	26,700
6.....	5,800	5,100
7.....	5,500	8,200
10.....	44,500	38,200

DOSES OF PENICILLIN

In the treatment of other diseases the following doses of penicillin generally have been considered adequate: for severe, acute infections with hemolytic streptococci or Staphylococcus aureus, about 120,000 to 240,000 Oxford units daily for ten to fourteen days, the total dose being from 500,000 to 1,000,000 or more units; for severe chronic infections such as osteomyelitis and

compound infected fractures, about 120,000 Oxford units daily.[4] Recent reports have indicated that doses somewhat smaller than those mentioned are generally effective: for severe infections with or without bacteremia, 48,000 to 160,000 Oxford units daily; for chronic infections 60,000 or more Oxford units daily. Indeed, one experienced investigator (Herrell)[5] has stated that a daily dose of from 40,000 to 60,000 (occasionally 100,000) Oxford units is entirely adequate, even for severe infections.

In the light of the foregoing, and in view of our policy of giving doses that might be considered more than sufficient rather than too low, we administered penicillin as follows: The first 2 patients received 320,000 units daily for the first five days, then 160,000 units daily for the next ten days. In addition, the second patient received 25,000 units intra-articularly (into a knee) on two successive days, making the total dose in the first 2 cases respectively 3,200,000 and 3,250,000 Oxford units over a period of fifteen days.

In view of the negative results in these first 2 cases, it was decided to treat the next 2 patients daily for one month, if possible. They were given daily doses of 160,000 units but, at the end of twenty days, it seemed wise to stop the injections, since no results were apparent and the patients were becoming "needle shy." Thus in case 3 as well as in case 4 a total of 3,200,000 units was given over a period of twenty days.

In the remaining 6 cases the doses were 240,000 units for the first day and 120,000 units daily thereafter for thirteen more days, a total of 1,800,000 units for each patient within fourteen days.

In each case the penicillin was given intramuscularly in divided doses, one dose every three hours day and night (table 1).

RESULTS

To evaluate our results critically we used a modification of a special research examination chart described elsewhere.[6] Every so often (before, during and after treatment), notations were carefully made as to articular swelling and tenderness, pain at rest, pain on voluntary and on forced motion of joints, limitation of motion and size of joints (measured with tape). Each examination sheet was filed away and was not studied until the courses of treatment had been concluded; in this way we were not influenced by the previous examinations.

Results from penicillin were essentially negative (table 1). We cannot even report the "inevitable 75 per cent of cases improved," as is reported so frequently after a wide variety of treatments.[7] Throughout the course of treatment minor fluctuations in some of the articular characteristics were noted, as can be expected even in cases of rheumatoid arthritis in which treatment is not given. But, in general, what few changes occurred were insignificant.

Joints.—In 7 cases there was no significant objective or subjective improvement. One patient felt worse after two weeks of treatment. In 1 case (case 6) there was slight subjective but no definite objective improvement. In 1 case (case 8) there was moderate objective and subjective improvement during the two weeks of treatment; that is, slight but definite reduction of pain and tenderness of fingers and ankles. But the condition of the metatarsophalangeal joints was not definitely improved; the sedimentation rate had increased slightly, and the patient was by no means cured or even much improved in condition. In view of the capricious nature of rheumatoid arthritis, the improvement in this case must be regarded as unrelated to the penicillin.

Laboratory Data.—The sedimentation rates recorded in table 1 are the average of three contiguous (and almost similar) determinations made before treatment and two made after treatment. In no case were there changes in the rate which could not be explained on the basis of variations inherent in the test itself or of the minor fluctuations of the disease.

Leukocyte counts made on synovial fluid after treatment did not differ materially from those made before treatment (table 2).

General.—Six of the 10 patients noted definite improvement in appetite in the course of treatment; in 4 the increased appetite was sustained after discontinuance of administration of penicillin. It is problematic whether this improvement was a side effect from penicillin or the result of rest and diet in the hospital.

TOXIC REACTIONS

Fever, chills, urticaria or other toxic reactions did not develop in any of the cases. The only unpleasant feature noted was the transitory, mild to moderate intramuscular soreness at the sites of injection; for this no special applications were necessary.

SUMMARY AND CONCLUSIONS

1. Penicillin was given to 10 soldiers with early but progressive rheumatoid arthritis.

2. Large doses of penicillin were given intramuscularly every three hours day and night. The daily doses of penicillin were from 120,000 to 320,000 Oxford units; total doses were from 1,800,000 to 3,250,000 units within fourteen to twenty days. Such large doses are known to be adequate, indeed perhaps more than adequate, against even severe infections (with or without bacteremia) from hemolytic streptococci, Staphylococcus aureus and so forth.

3. Our clinical results from penicillin, given in the doses stated over a period of fourteen to twenty days, were essentially negative. In 7 of the 10 cases there was no significant subjective or objective improvement. One patient felt worse but did not appear to be in worse condition than before treatment. In 1 case there was slight subjective, but no definite objective, improvement. One patient experienced moderate objective and subjective improvement in some, but not in all, his affected joints; the sedimentation rate increased slightly during treatment, and he was by no means cured or even decidedly improved. In view of the capricious nature of rheumatoid arthritis the improvement in these 2 cases must be regarded as unrelated to the penicillin.

4. There was no definite evidence of improvement as measured by laboratory tests. There was no significant improvement in sedimentation rates or in the

4. Keefer, C. S.; Blake, F. G.; Marshall, E. K., Jr.; Lockwood, J. S., and Wood, W. B., Jr.: Penicillin in the Treatment of Infections: A Report of 500 cases; Statement by Committee on Chemotherapeutic and Other Agents, Division of Medical Sciences, National Research Council, J. A. M. A. **122:** 1217-1224 (Aug. 28) 1943.

5. Herrell, W. E.: Further Observations on the Clinical Use of Penicillin, Proc. Staff Meet., Mayo Clin. **18:** 65-76 (March 10) 1943; The Clinical Use of Penicillin: An Antibacterial Agent of Biologic Origin, J. A. M. A. **124:** 622-627 (March 4) 1944. Herrell, W. E.; Nichols, D. R., and Heilman, Dorothy H.: Penicillin: Its Usefulness, Limitations, Diffusion and Detection, with Analysis of 150 Cases in Which It Was Employed, ibid. **125:** 1003-1010 (Aug. 12) 1944.

6. Hench, P. S.; Slocumb, C. H., and Popp, W. C.: Fever Therapy: Results for Gonorrheal Arthritis, Chronic Infectious (Atrophic) Arthritis, and Other Forms of "Rheumatism," J. A. M. A. **104:** 1779-1790 (May 18) 1935.

7. Hench, P. S.; Bauer, Walter; Dawson, M. H.; Hall, Francis; Holbrook, W. P., and Key, J. A.: The Problem of Rheumatism and Arthritis: Review of American and English Literature for 1937 (Fifth Rheumatism Review), Ann. Int. Med. **12:** 1092 (Jan.) 1939.

comparative leukocyte counts on synovial fluid, made before and after treatment.

5. Definite improvement in appetite was noted by 6 of the 10 patients. It may have been unrelated to treatment with penicillin or it may have been a general side effect thereof.

6. Our results offer no support to the idea that hemolytic streptococci may be etiologically related to rheumatoid arthritis.

7. In view of these negative results with rather large doses of penicillin, it does not seem unreasonable to assume that rheumatoid arthritis is not caused by any of the bacteria which are already known to be rapidly affected by penicillin.

8. From these negative results we would conclude that penicillin probably should not be used for the further clinical treatment of rheumatoid arthritis, at least until the material is available in something approaching inexhaustible quantities. Further researches with penicillin in rheumatoid arthritis may be in order. At present the limited supplies available for clinical use should be allotted for the treatment of patients with diseases in which curative results are more likely to eventuate than in rheumatoid arthritis.

THE EFFECT OF VITAMIN SUPPLEMENTS ON NORMAL PERSONS

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AND
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At the present time the use of vitamins is widespread throughout the country, not only in the treatment of disease, but also by apparently normal persons. While no one would question the employment of vitamin therapy in frank deficiency diseases or even in suspected deficiency states, still one wonders if the indiscriminate use of vitamins, sold over the counter to people who have no obvious disease, is justified. It has been argued that such vague symptoms as weakness, nervousness, fatigability and insomnia can result from a vitamin deficiency and therefore, when such symptoms appear, vitamin therapy should be instituted.[1] Recent surveys, with the recommended daily allowances of the National Research Council as a guide, have indicated that the average American diet often is not adequate to maintain optimal nutrition.[2] This has been used as an additional argument for the administration of vitamins to people without obvious disease on the assumption that they may actually have a "subclinical deficiency" of which they are not aware.[3] It has been implied that, even when no demonstrable deficiency exists, one's sense of well-being and ability to perform work can be improved greatly by the addition of vitamins to the diet. As pointed out by the Councils on Food and Nurtition and on Industrial Health there is at present no conclusive evidence to substantiate this point of view.[4] In an effort to determine the effect, if any, of various vitamin supplements on apparently normal persons, the following study was undertaken.

From the Department of Medicine, Duke University School of Medicine.

This study was conducted at the request of the Office of the Quartermaster General, U. S. Army.

1. Haggard, H. W.: Should War Workers Be Fed Vitamins? in The Nutrition Front: Report of the New York State Joint Legislative Committee on Nutrition, Legislative Document No. 64, Albany, N. Y., 1943.
2. Recommended Dietary Allowances, Report of Food and Nutrition Board, National Research Council, January 1943.
3. Nutritional Deficiencies in the United States, Nutrition Rev. **2**: 227-230 (Aug.) 1944.
4. Indiscriminate Administration of Vitamins to Workers in Industry, Report of Council on Foods and Nutrition and Council on Industrial Health, J. A. M. A. **118**: 618-621 (Feb. 21) 1942.

METHOD

Volunteer medical students and technicians were used as subjects. They all continued their usual activities and ate essentially the same diet. Each subject was given a work sheet to be kept daily and was instructed to record his impression as to the effect of the medication he was taking on the appetite, energy and "pep," general health, "gas" or indigestion, nausea, vomiting, the number of stools per day, abdominal pain and weight. Extraneous factors which might possibly have affected the subject also were noted. A code was printed on the work sheet to insure uniformity of recording. The time of the experiment was purposely placed in the midterm to avoid the factor of examinations. The duration was one month during which each subject took his supplements daily. No subject knew what he was receiving or to what group he belonged. At the beginning of the experiment they were told that one group would receive placebos and the remainder various vitamins. They were instructed not to compare notes or discuss their symptoms with fellow subjects.

TABLE 1.—*Supplements for Each Group*

Group A—Vitamin tablets	3 per day
Liver extract tablets	6 per day
Group B—Vitamin tablets	3 per day
Yeast extract tablets	6 per day
Group C—Vitamin tablets	3 per day
Placebos	6 per day
Group D—Vitamin tablets	3 per day
Group E—Placebos	6 per day

Two hundred subjects were selected and divided into five groups. The supplements for each group were shown in table 1. The supplements used were of the same size and appearance, so that identification was difficult, if not impossible, without chemical analysis.

The contents of the various supplements were:

Vitamin tablets:[5] vitamin A, 2,500 U. S. P. units; vitamin D, 200 U. S. P. units; thiamine hydrochloride, 1 mg.; riboflavin, 1.5 mg.; ascorbic acid, 27.5 mg.; nicotinamide, 10 mg.

Liver extract tablets, 0.5 Gm. of Wilson's liver extract 1:20.

Yeast extract tablets, 0.5 Gm. of dried yeast extract.

Placebos, dextrose.

TABLE 2.—*Appetite*

Supplement	Group A Vitamins and Liver Extract	Group B Vitamins and Yeast	Group C Vitamins and Placebos	Group D Vitamins	Group E Placebos
Improved	6	3	9	5	5
Unchanged	31	32	24	28	29
Decreased	0	3	2	2	1
Total	37	38	35	35	35

The coating of the tablets was gelatin cane sugar with iron oxide as a coloring matter.

Reliable data were obtained from 182 subjects, the number in each group being shown in the accompanying tables.

Appetite.—The appetite was indicated as improved, unchanged or decreased. The subject was classified as having an improvement or impairment of appetite only

5. The vitamin tablets were the usual government issue and furnished by the Office of the Quartermaster General. The remainder of the supplements were furnished through the courtesy of the Vi-Co Products Company, Chicago.

in those cases in which definite and significant changes were recorded. The findings are shown in table 2. It will be seen that there is no essential difference among the various groups.

Energy and "Pep," General Health and Weight.—The same method of classification was employed in evaluating energy and "pep," general health and weight (tables 3, 4 and 5). It will be observed that the number recording improvement in energy and "pep" and in general health, as well as gain in weight, was essentially the same in the group taking placebos as in the other four groups who were taking various vitamin supplements.

TABLE 3.—*"Energy and Pep"*

Supplement	Group A Vitamins and Liver Extract	Group B Vitamins and Yeast	Group C Vitamins and Placebos	Group D Vitamins	Group E Placebos
Improved	5	5	5	7	6
Unchanged	29	32	28	28	27
Decreased	3	1	2	0	2
Total	37	38	35	35	35

TABLE 4.—*General Health*

Supplement	Group A Vitamins and Liver Extract	Group B Vitamins and Yeast	Group C Vitamins and Placebos	Group D Vitamins	Group E Placebos
Improved	1	2	1	1	2
Unchanged	35	37	34	34	33
Total	36	39	35	35	35

"Gas" and Indigestion and Abdominal Pain.—These symptoms were recorded as being present or absent. Here again, unless the changes were definite and unmistakable, they were not classified as being present. The results are shown in tables 6 and 7. No significant differences were noted in the symptoms "gas and indigestion" by the various groups. However, in the group taking yeast there was a definite increase in the number of subjects who recorded the development of abdominal pain.

TABLE 5.—*Weight*

Supplement	Group A Vitamins and Liver Extract	Group B Vitamins and Yeast	Group C Vitamins and Placebos	Group D Vitamins	Group E Placebos
Increased	6	1	1	5	5
Unchanged	24	35	33	28	29
Decreased	8	3	0	2	0
Total	38	39	34	35	34

TABLE 6.—*"Gas" and Indigestion*

Supplement	Group A Vitamins and Liver Extract	Group B Vitamins and Yeast	Group C Vitamins and Placebos	Group D Vitamins	Group E Placebos
Present	5	6	3	1	5
Absent	31	32	31	35	30
Total	36	38	34	36	35

Nausea, Vomiting and Diarrhea.—Except for 1 subject taking placebos, nausea and vomiting occurred only in those taking liver extract and yeast, particularly the liver extract. Likewise diarrhea developed most frequently in those taking liver and yeast (tables 8 and 9).

STATISTICAL ANALYSIS

A statistical analysis of the data was made using the chi square test.[6] In analyzing the effects of the supplements in the five respective groups, only six comparisons indicated real or significant differences. These were noted in nausea and vomiting, abdominal pain and diarrhea. A significant increase in diarrhea and a highly significant increase in abdominal pain and in nausea and vomiting occurred in those groups receiving liver extract and yeast. No significant difference was noted in appetite, energy and "pep," "gas" and indigestion, general health or weight among the various groups.

TABLE 7.—*Abdominal Pain*

Supplement	Group A Vitamins and Liver Extract	Group B Vitamins and Yeast	Group C Vitamins and Placebos	Group D Vitamins	Group E Placebos
Present	6	9	3	1	1
Absent	30	30	31	34	34
Total	36	39	34	35	35

TABLE 8.—*Nausea and Vomiting*

Supplement	Group A Vitamins and Liver Extract	Group B Vitamins and Yeast	Group C Vitamins and Placebos	Group D Vitamins	Group E Placebos
Present	8	2	0	0	1
Absent	29	36	34	35	34
Total	37	38	34	35	35

TABLE 9.—*Diarrhea*

Supplement	(Three or More Stools per Day) Group A Vitamins and Liver Extract	Group B Vitamins and Yeast	Group C Vitamins and Placebos	Group D Vitamins	Group E Placebos
Present	8	6	3	1	4
Absent	27	32	31	34	31
Total	35	38	34	35	35

COMMENT

Our purpose in this study was to obtain impartial and intelligent daily records of the effect of various vitamin supplements on apparently normal persons. It was felt that in such a study medical students would be not only cooperative but critical as well. The duration of the experiment was set arbitrarily at thirty days. In our experience, patients having frank deficiencies recover rapidly when specific therapy is instituted. It is reasonable to assume that a subclinical deficiency should respond just as promptly to treatment, and therefore it was felt that nothing would be gained by prolonging the experiment.

All of the subjects were consuming the usual American diet and apparently were in good health. Before beginning the experiment 20 of them, selected at random, had vitamin studies made, including the determination of carotene, vitamins A and C, nicotinic acid, thiamine hydrochloride, riboflavin, pyridoxine, pantothenic acid and prothrombin time. All of these were within normal limits.

6. The Office of the Quartermaster General prepared this statistical study.

The selection of appetite, energy and "pep" and general health for evaluation was based on the assertion that vitamins will stimulate the appetite, increase energy and "pep" and improve the general health even in apparently normal persons. Our own experience suggested that untoward symptoms might arise following the administration of yeast or liver extract. Therefore "gas," indigestion, nausea, vomiting, abdominal pain and diarrhea were included in the work sheet.

As already stated, the greatest care was exercised in the evaluation of changes noted by the subject. Only when these were definite and unmistakable were they recorded as such. The evaluation of the data submitted by each subject was made without knowledge of what supplement he had been taking.

It is well known that yeast and liver extract occasionally may cause distressing gastrointestinal symptoms, and this was confirmed by the observations reported in this study. The same beneficial effect was noted on the appetite, energy and "pep," general health and weight in the group taking placebos as in the groups taking the various vitamin supplements.

SUMMARY

The administration of vitamin supplements to a group of apparently normal persons, consuming the usual American diet, had no demonstrable beneficial effect.

INTERSTITIAL CYSTITIS OF MEN

A REVIEW OF SEVENTY-EIGHT CASES

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Ever since Hunner [1] described the clinical picture of ulcer of the bladder in women which has since borne his name, relatively few cases involving men have been described. Peterson and Hager [2] demonstrated the general incidence of interstitial cystitis by reporting 8 cases, all involving women, from a series of 1,707 urologic patients. This group was made up of 1,292 men and 415 women. While most of the patients have been women, this disease has been observed among men by many investigators. In a series of 14 cases reported in 1922, Kretschmer [3] described 1 case in a man. In 1929 Hinman [4] reported 6 cases in men in a series of 110 cases. Two of the 15 cases that Bumpus [5] reviewed in 1930 were in men. In 1932 Folsom [6] described his series of 20 cases of interstitial cystitis, 3 of which were in men. In 1935 Young [7] reviewed 45 cases, of which 41 were in women and 4 in men. Higgins [8] reviewed 100 cases in 1941, 6 in men.

We are presenting some observations derived from reviewing the records of 78 cases of interstitial cystitis involving men. It is interesting that from an original group of 113 cases accumulating over a period of twenty-six years in which a diagnosis of interstitial cystitis had been made, only 2 have proved subsequently to be cases of vesical neoplasm and 1 eventually proved to be a case of tuberculous cystitis. Of the original group we selected 78 cases in which we have follow-up information which corroborates the diagnosis of interstitial cystitis. The remaining 32 cases are not included in this report because we did not believe that the diagnosis of interstitial cystitis was established unequivocally.

ETIOLOGY

The causation of interstitial cystitis is still a mystery. As in many other conditions in which the etiologic agent is not definitely established, focal infection has received its share of consideration. Hunner, as well as Meisser and Bumpus,[9] favored the hypothesis of the focal origin of this disease. However, Keene [10] was unable to produce even symptomatic relief after carefully eradicating all foci of infection. Hinman made a careful search for foci of infection in the 110 cases that he reviewed. In 80 per cent of the cases induced abortions, ectopic pregnancies, pelvic inflammatory disease or pronounced menstrual irregularity had occurred. Of his 6 male patients, 3 had a positive history of gonorrhea and 1 had syphilis with a primary genital chancre. Higgins found disease of the upper part of the urinary tract, such as pyelonephritis, hydronephrosis or infected hydronephrosis, to be present in 19 per cent of 100 cases. Of the 6 men in Higgins's group, 3 had coexisting prostatitis and 1 had syphilis. Meads [11] considered neglected cystitis as ranking with foci of infection as an etiologic agent. Nelson and Pinard [12] stated that practically all men suffering from interstitial cystitis have pyogenic infection of the prostate and seminal vesicles. Young [7] reported that 2 patients were completely cured after eradication of chronic prostatitis.

In our series 11 (14 per cent) men had coexisting chronic prostatitis. In 5 of the 67 cases in which the upper part of the urinary tract was investigated there were chronic inflammatory changes of the kidney and ureters, in 1 there was rather active bilateral pyelonephritis and in 2 there were small, asymptomatic renal calculi. Twenty-six patients (33 per cent) gave a positive history of previous gonorrheal infection, while 48 patients (62 per cent) denied any such history. Urethral strictures were present in 8 cases (10 per cent) and previous abdominal operations had been performed in 9 (12 per cent) of the cases.

This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the U. S. Navy. The opinions and views set forth in this article are those of the writers and are not to be considered as reflecting the policies of the Navy department.

1. Hunner, G. L.: A Rare Type of Bladder Ulcer in Women: Report of Cases, Tr. South. Surg. & Gynec. A. **27:** 247-288, 1914.
2. Peterson, Anders, and Hager, B. H.: Interstitial Cystitis: Report of Cases, California & West. Med. **31:** 262-266 (Oct.) 1929.
3. Kretschmer, H. L.: Elusive Ulcer of the Bladder, Surg., Gynec. & Obst. **35:** 759-765 (Dec.) 1922.
4. Hinman, Franklin, discussion on Peterson and Hager,[2] p. 267.
5. Bumpus, H. C., Jr.: Interstitial Cystitis: Its Treatment by Overdistention of Bladder, M. Clin. North America **13:** 1495-1498 (May) 1930.
6. Folsom, A. I.: Hunner's Ulcer, Texas State J. Med. **27:** 718-721 (Feb.) 1932.
7. Young, J. E., Jr.: Hunner Ulcer of the Bladder, Cleveland Clin. Quart. **2:** 51-54 (Jan.) 1935.
8. Higgins, C. C.: Hunner Ulcer of the Bladder (Review of 100 Cases), Ann. Int. Med. **15:** 708-715 (Oct.) 1941.
9. Meisser, J. G., and Bumpus, H. C., Jr.: Focal Infections in Relation to Submucous Ulcer of the Bladder and to Cystitis, J. Urol. **6:** 285-298 (Oct.) 1921.
10. Keene, F. E.: Circumscribed Pan Mural Ulcerative Cystitis: Elusive Ulcer (Hunner), Ann. Surg. **71:** 479-485 (April) 1920.
11. Meads, A. N.: Hunner Ulcer, Urol. & Cutan. Rev. **38:** 631-634 (Sept.) 1934.
12. Nelson, O. A., and Pinard, C. J., Jr.: Interstitial Cystitis, Northwest Med. **40:** 230-233 (July) 1941.

INCIDENCE

Interstitial cystitis is predominantly a disease of women. Most authorities estimate that it is four times as common among women as among men. Our experience essentially bears out this information. Symptoms began between the ages of 20 and 59 years in 64 (82 per cent) of our 78 cases in men. We have observed that

Fig. 1.—Thinned vesical epithelium and subepithelial inflammatory changes; slightly reduced from a photomicrograph with a magnification of 13 diameters.

in the reported cases men were generally younger at onset of symptoms than women. The earliest onset of symptoms in our series was at the age of 16 years. The oldest was at the age of 74 years.

PATHOLOGY

Specimens of the vesical wall were available for microscopic examination in 17 of our cases. These examined specimens were from the cases in which

Fig. 2.—Inflammatory changes within the subepithelial connective tissue, slightly reduced from a photomicrograph with a magnification of 30 diameters. Increased vascularity, collections of leukocytes and erythrocytes and varying degrees of edema.

biopsy, segmental resection or total cystectomy had been performed. A pathologist confirmed our diagnosis in each of these cases. Following is a description of the pathologic characteristics of interstitial cystitis written by Dr. Broders.[13]

13. Dr. Broders is head of the Section on Surgical Pathology in the Mayo Clinic and professor of pathology in the Mayo Foundation, Graduate School, University of Minnesota.

Little can be added to Hunner's description of the pathologic process in the urinary bladder variously designated "Hunner's ulcer," "submucous ulcer," "elusive ulcer," "paracystitis," "panmural ulcerative cystitis" and "chronic interstitial cystitis." The process is an inflammation of the connective tissue of the bladder that is by far most pronounced, and apparently primary, in the subepithelial connective tissue. This layer consists of the connective tissue of the mucosa and the so-called submucosa, and it lies between the epithelium and the musculature. The inflammatory process extends to the epithelium, intermuscular connective tissue, musculature, serosa or adventitia.

When the lesion is removed and examined, the inflammation is found to be in a chronic state. However, it would be contrary to sound reasoning to assume that the inflammation is chronic from the outset. It seems reasonable to assume, therefore, that the inflammatory process passes through acute, subacute and chronic phases and that there are exacerbations of acute and subacute phases which tend to intensify the chronic phase.

The involved portion of the wall of the bladder is thickened; however, the epithelial layer is for the most part thinned (fig. 1), so that areas exist in which the epithelium is only one or two cell-layers thick and, in other areas, the epithelium is destroyed and superficial ulceration remains.

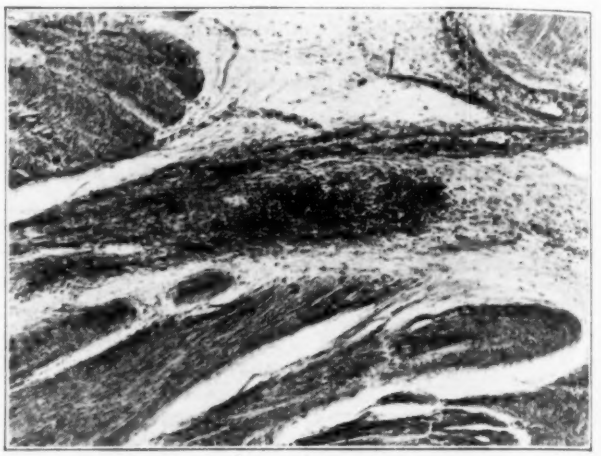

Fig. 3.—Collections of inflammatory cells within the intermuscular connective tissue, slightly reduced from a photomicrograph with a magnification of 80 diameters.

In the subepithelial connective tissue, where the inflammation is most pronounced, the characteristics are as follows: increased vascularity; numerous lymphocytes, mostly small lymphocytes; a fair number of polymorphonuclear leukocytes both within and without the blood and lymph vessels and spaces; a few monocytes and plasma cells; numerous erythrocytes within and without the blood vessels and blood spaces, and varying degrees of edema (fig. 2). In other words, the process is comparable to that found in the inflammatory granulating base of a chronic excavated ulcer of the urinary bladder or stomach.

The inflammatory process in the intermuscular connective tissue (fig. 3), musculature, serosa or adventitia is less pronounced than that in the subepithelial connective tissue. The serosa or adventitia is usually thickened. The musculature may be distorted to some extent; however, there is very little loss of continuity of the musculature, in contrast to the marked loss of continuity found in an excavated ulcer of the bladder or stomach.

In some lesions there is very little increase of fibrous connective tissue, while in others the increase is so marked as to produce real fibrosis throughout the vesical wall with or without hyaline degeneration. The amount of fibrosis is probably in direct proportion to the duration of the inflammatory process. The process as a whole resembles closely that relatively rare lesion of the stomach known as "linitis plastica of non-neoplastic type."

SYMPTOMS

The most distressing symptoms of interstitial cystitis are highly characteristic regardless of the sex. Most prominent is "clocklike" urinary frequency with urgent voidings approximately every two hours during day and night. Almost equally distressing and universal is lower abdominal suprapubic or perineal pain relieved by voiding small amounts of urine and aggravated by jarring or overdistention of the bladder. These symptoms predominated in our series. Hematuria noted prior to treatment or examination occurs fairly often and has been noted in 18 per cent of Higgins's [8] series, in 13 of Kretschmer's [3] 44 reviewed cases and in 20 per cent of the cases reviewed by Smith and Conroy.[14]

In our series 24 patients (31 per cent) gave a history of terminal gross hematuria. Burning, urgency and vesical tenesmus were occasional complaints. Obstructive urinary symptoms of varying degrees were present in 14 (18 per cent) of our cases. While one would expect obstructive urinary symptoms to affect some of any such group of male patients, it is interesting that in several cases, after a transurethral prostatic operation had been performed, the obstructive symptoms persisted and were relieved only after the interstitial cystitis had been discovered and treated. The report of case 2 illustrates this point. It is also interesting that obstructive symptoms have been observed among women.

DIAGNOSIS

The diagnosis of interstitial cystitis is established by the patient's characteristic history together with rather typical cystoscopic findings. The more important findings include reduction of vesical capacity, ideally a urine free from pus, blood or organisms unless the patient has had previous treatment or accompanying urologic pathologic changes, and a rather typical cystoscopic appearance of the bladder which will vary to a great extent depending on the degree of healing present. The most characteristic cystoscopic finding is one or more discrete salmon pink, shrimp or Russian dressing colored areas found mostly on the apex or dome but frequently on any area of the bladder except the trigone. Instrumental palpation of these areas will produce the identical pain that the patient has described in the case history. Overdistention of the bladder produces a linear splitting with associated hemorrhages of the mucosa overlying these areas. Finally, most patients will obtain symptomatic relief from overdistention of the bladder, lavage with increasing concentrations of silver nitrate, fulguration of the involved mucosa or a combination of these procedures. Cases in which essentially all of these features were observed we regarded as typical. Cases in which other urinary complaints were recorded or in which these findings were lacking we arbitrarily considered as being atypical. We insisted on all the cystoscopic findings for the diagnosis, and in every case the opinion of at least two cystoscopists was obtained.

The data in 64 (82 per cent) of the 78 cases were typical, while the data in the remaining cases were considered as being atypical because of additional obstructive symptoms. In only 16 (21 per cent) of our cases was the urine free from pus, blood and organisms. It is interesting to note that in these cases there had been no previous cystoscopy or treatment. In 37 cases (47 per cent) 0 to 15 pus cells per high power field were observed in the initial examination of the urine, while in 34 cases (44 per cent) 15 to 40 pus cells were observed which were negative to Gram's stain. Positivity to Gram's stain and positive culture of the urine were present in 7 cases (9 per cent). Of the latter group there were 3 cases in which Escherichia coli was cultured, 2 cases in which Pseudomonas was cultured and 2 cases in which Streptococcus fecalis was cultured. In 1 of the cases in which Escherichia coli was cultured, gram-negative bacilli were recovered from both kidneys and the disease in this case was considered to be active bilateral pyelonephritis with interstitial cystitis. As had been pointed out by Hinman,[4] Higgins [8] and others, the high percentage of patients suffering from pyuria can be attributed to previous treatment and instrumentation.

Interstitial cystitis in both sexes is to be distinguished from so-called simple ulceration, tuberculous ulceration, the accompanying inflammation of an underlying neoplasm and mucosal lesions resulting from extravesical lesions and, among women, from ulceration following application of radium to the cervix or vagina. We considered it necessary to exclude tuberculosis in 67 (86 per cent) of the cases.

TREATMENT

We have relied chiefly on vesical overdistention or on instillation into the bladder of increasing concentrations of silver nitrate. The former method is usually selected in cases of severe interstitial cystitis in which prompt relief is desired. It is our impression that overdistention with the patient under local anesthesia is useless; this procedure requires either intravenous or spinal anesthesia. Our method of vesical overdistention consists in distending the bladder under vision until actual "splitting" of the mucosa which overlies the region or regions of interstitial cystitis is noted. During the process the affected regions are kept under constant inspection and the first evidence that "splitting" is about to occur is a bluish white discoloration of the mucosa. Actual splitting occurs shortly thereafter and is followed by bleeding from the site of rupture. The amount of fluid necessary to produce splitting varies from 200 to 800 cc., and the procedure can be repeated safely at intervals. Usually, superficial fulguration of the regions of interstitial cystitis is carried out. At times overdistention is supplemented by the use of continuous vesical lavage with increasing concentrations of silver nitrate.

Dramatic results may be obtained by the use of silver nitrate. The method we employ consists in the instillation of 1 to 2 ounces (30 to 60 cc.) of solution of silver nitrate into the bladder daily. At the outset a 1:3,000 solution is employed, and the concentration is increased gradually until 1 per cent solution of silver nitrate can be tolerated. The solution is instilled into the bladder by means of a catheter, allowed to remain in place for five minutes and then drained off through the catheter. We do not employ any local anesthetic agents, although it may be necessary to prescribe codeine or belladonna and opium suppositories if the treatment results in unusual pain. When the proper concentration has been reached and the patient is comfortable, it may be possible to keep him in that condition by the monthly or bimonthly instillation of 1:1,000 or 1:2,000 solution of silver nitrate. Segmental resection, subtotal cystec-

14. Smith, E., and Conroy, F. D.: Interstitial Cystitis, Canad. M. A. J. 45:342-345 (Oct.) 1941.

tomy, presacral neurectomy and the instillation of mild protein silver, phenol or alcohol are mentioned simply for the sake of completeness.

REPORT OF CASES

In the reports of the cases which follow, the first illustrates a rather typical case. The second illustrates the fact that obstructive urinary symptoms which were not relieved by a prostatic operation were relieved by treatment of the interstitial cystitis.

CASE 1.—A white man aged 35, a school teacher, registered at the Mayo Clinic on Dec. 27, 1933 complaining of day and night urinary frequency associated with an aching discomfort in the bladder and urethra. These symptoms first had begun three years before and had been becoming constantly more severe. In February 1932 cystoscopy had been performed and the patient had been told that he suffered from interstitial cystitis. A left pyelogram was made at the same time and no abnormalities were noted. Tuberculosis had been excluded by acid fast stains and inoculations of guinea pigs. Vesical overdistention and lavage had been performed repeatedly without improvement. One physician had found that the patient had prostatitis and administered many prostatic massages, which did not affect the patient's symptoms. On the recommendation of his physician his tonsils were removed. The patient's history by symptoms, as well as his family history, was noncontributory. His past medical history was also of no significance and he stated that he had never had gonorrhea.

The results of general physical examination were essentially negative. Urinalysis revealed 7 pus cells per high power field of the microscope. The erythrocyte count, the leukocyte count and the value for hemoglobin were within normal limits. The prostatic secretion appeared normal. Results of the flocculation test for syphilis and roentgenograms of the thorax and pelvis were all negative. Cystoscopy with the patient under pentothal sodium anesthesia revealed an area of interstitial cystitis involving the posterior wall and extending up to the dome. The vesical capacity was 150 cc. The bladder was overdistended with 475 cc. of water to produce splitting of the mucosa over the involved areas. Vesical overdistention was repeated twice more at six day intervals and the patient was given vesical lavage, was instructed to follow a ketogenic diet and was dismissed with only moderate relief of symptoms.

The patient returned to the clinic on Feb. 15, 1939 with symptoms similar to those at the time of his first visit after having been free from symptoms in the intervening six years. Cystoscopy performed the next day with the patient under pentothal sodium anesthesia disclosed a typical region of interstitial cystitis on the left wall of the bladder measuring approximately 3 cm. in diameter and another on the right lateral wall measuring approximately 2 cm. in diameter. The bladder was overdistended to 225 cc. with characteristic splitting and hemorrhage in both regions. Specimens taken at this time for biopsy were reported as being "inflammatory tissue." The patient was given a course of emetine, and instructions were sent to his local physician for administering the second course of treatment.

The patient returned on Aug. 27, 1940 complaining of a return of the original symptoms, after sixteen months of considerable improvement. Since he could not remain here, he was referred to his local urologist for overdistentions of his bladder to be performed at intervals.

CASE 2.—A white man aged 42 presented himself at the clinic on Sept. 23, 1942 complaining of periodic dysuria, urinary frequency, nocturia and perineal pain that had begun in 1932. These symptoms had progressed and become more severe, so that by April 1942 he was voiding small amounts of urine every hour during the day and six times during the night, suffering from considerable dysuria and perineal pain, and experiencing hesitancy with narrowing of the urinary stream. He consulted a urologist in his home town, and transurethral prostatic resection was performed in April 1942. His postoperative course was uneventful but his symptoms were unaffected. Since that time his home physician had been giving him vesical lavages and urethral dilations. The patient had suffered a definite attack of gonorrhea seventeen years and a questionable attack of gonorrhea seven years before. Appendectomy had been performed in 1927.

Results of general physical examination were essentially negative. Urinalysis revealed 4 pus cells and an occasional erythrocyte per high power field of the microscope. A culture of the urine was negative. There was 20 cc. of residual urine. The erythrocyte count, leukocyte count and value for hemoglobin were within normal limits. Results of the flocculation test for syphilis were negative. The blood urea was 26 mg. per hundred cubic centimeters of blood. Roentgenograms of the thorax and colon did not reveal any abnormalities. The prostatic secretion was normal. An excretory urogram was negative. Cystoscopy performed with the patient under intravenous pentothal sodium anesthesia disclosed a typical region of interstitial cystitis on the dome of the bladder just anterior to the air bubble. The prostatic urethra and the vesical neck appeared normal. The bladder was overdistended to 425 cc., resulting in bleeding and rupture of the mucosa at the site of the region of cystitis. A course of lavage of the bladder with silver nitrate was given. By Oct. 12, 1942 the patient was voiding a good stream without dysuria and his nocturia was reduced 50 per cent.

The patient returned to the clinic on April 14, 1943 complaining of a recurrence of his urinary symptoms but to a less severe degree than formerly. The results of physical examination and the laboratory findings were similar to those of the earlier admission. Repeated examinations of his urine for the tubercle bacillus were negative. On April 19, 1943 cystoscopy was done with the patient under intravenous pentothal sodium anesthesia, and a region of interstitial cystitis was found in the right side of the dome. This region was seen to have torn and bled after the bladder had been overdistended with 600 cc. of water and was then lightly fulgurated. Symptomatic improvement was almost immediate and the patient was given a further course of lavage with silver nitrate. The patient requested and was granted another overdistention of the bladder. He was dismissed as greatly improved on May 13, 1943. The patient wrote to us on Aug. 30, 1943 and stated that he was feeling entirely well.

SUMMARY AND CONCLUSIONS

On the basis of a review of data on 78 cases of interstitial cystitis of men the following conclusions are drawn:

1. Although interstitial cystitis is predominantly a disease of women, it is found to have a significant incidence among men. A search for evidence of interstitial cystitis among male patients will explain a number of cases of puzzling and intractable cystitis.

2. The clinical picture among male patients is often deceiving because of accompanying obstructive symptoms, especially in the prostatic age group.

3. Still more deceiving are the cases in which obstructive symptoms are superimposed without any obstructive pathologic change. In these cases the obstructive symptoms are part of the picture of cystitis and will be found to be relieved by treatment of the cystitis rather than by a prostatic operation.

A Great Figure in Syphilology.—Phillipe Ricord (1800-1889) is one of the great figures in syphilology. He was an investigator of the first rank and he is another illustration of the men who have been most fruitful in original scientific work while carrying the burdens of an enormous practice. He rose from poverty to large wealth and became one of the most popular and influential citizens of Paris. He was born in Baltimore and until he was 20 lived in the United States, but the only claim the United States can make upon him is that it gave his father's family refuge in time of revolution and afforded him an opportunity to get his preliminary education and to study natural history under his uncle.—Pusey, William Allen: The History of Dermatology, Springfield, Ill., Charles C Thomas, 1933.

TRANSIENT HYPERTENSION

ITS SIGNIFICANCE IN TERMS OF LATER DEVELOPMENT OF SUSTAINED HYPERTENSION AND CARDIOVASCULAR-RENAL DISEASES

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For many years the significance of transient hypertension has been a topic of discussion. As long ago as 1921 Fahrenkamp [1] and Kylin [2] independently noted that excessive variability of the blood pressure, with temporary rises above the usual normal, sometimes was found in the early stages of hypertensive vascular disease. A little later Fahrenkamp [3] stressed the importance of psychic disturbances as a cause of such vasomotor instability. More recently, numerous authors have presented data in support of the view that transient elevations of blood pressure, induced by emotion or some other stimulus, should be regarded as evidence of a possible prehypertensive state.[4] But the number of cases studied has been relatively small, the periods of observation usually have not been long and no records have been kept between their beginning and end. Inferences drawn from insurance statistics are based almost entirely on mortality experience following a single reading and so have a limited value.

In examinations of registrants for military service transient hypertension, presumably due to nervousness, has been commonly encountered and examiners have varied in their judgment as to its importance.[5] Mobilization Regulations prescribe that if the blood pressure appears to be abnormally high it is to be measured after the subject has rested in the recumbent position. The decision as to the acceptability of the selectee is left to the physician, who is permitted to disregard a persistent pressure of over 150 mm. of mercury systolic or over 90 diastolic if, in his opinion, the rise is due to psychic reaction and is not secondary to renal or other systemic disease. It is our purpose in this study to inquire into the validity of these criteria by critical analysis of the medical records of 22,741 army officers. In the course of the discussion facts believed to apply to the general male population of comparable physical fitness and similar age groups will become evident.

MATERIAL, DEFINITIONS AND PROCEDURE

In a previous paper [6] were described the sources of the 22,741 records on which this analysis is based, the general character of the material and the scheme followed in preparing it for study. The manner in which the blood pressures were taken and the points at which systolic and diastolic levels were measured is not known. Errors and variations in either direction were probably not great, and it is fair to assume that in such a large series of readings they canceled one another.

Definition of the terms employed is necessary for clear understanding. By transient hypertension is meant a reading of over 150 mm. of mercury systolic or 90 diastolic which is followed, on any particular examination or at a later examination, by a reading below these levels. The highest systolic and diastolic readings obtained in any one of a series made at a given examination were recorded. Sustained hypertension is taken to mean a reading of over 150 systolic or over 90 diastolic persisting throughout an examination and not followed in subsequent examinations by lower levels. A persistent elevation of either systolic or diastolic pressure on a final examination, even though this marked its first appearance, is considered to represent sustained hypertension.

Cardiovascular-renal diseases were grouped and included those conditions due to vascular degeneration which involved brain, heart or kidneys. Cerebral hemorrhage and thrombosis, hypertension, the various manifestations of coronary heart disease and chronic nephritis and uremia were the most frequent diagnoses. Rheumatic heart disease, bacterial endocarditis, syphilitic aortitis and disturbances due to thyrotoxicosis were excluded. In the tables dealing with disability retirement and death rates, both primary (basic) and secondary (immediate) causes were included. In other words, the presence of a cardiovascular-renal condition always was recorded, even though it was not directly responsible for retirement or death.

The group of neuropsychiatric disorders comprised chiefly psychoneuroses, psychoses (including the psychosis due to alcohol), manic depressive psychosis, dementia precox and mental disturbances due to cerebral arteriosclerosis (these patients often were classed merely as "mentally unsound"); it included deaths due to suicide. A few cases of tabes dorsalis and dementia paralytica were not placed in this category but were listed under the diagnosis of syphilis.

In dealing with data of this sort, age is of fundamental importance and in each table the figures are given according to age groups. The actuarial summaries (tables 7 and 8) are of necessity based on cumulative figures derived from these groups. In order to

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This is the second in a series of papers dealing with "Studies of Blood Pressure in Army Officers."

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Columbia University.

Dr. John W. Fertig, professor of biostatistics, Columbia University College of Physicians and Surgeons, aided in the analysis and preparation of the material for final presentation.

Read before the Section on Practice of Medicine at the Ninety-Fourth Annual Session of the American Medical Association, Chicago, June 15, 1944.

1. Fahrenkamp, Karl: Beitrag zur Kenntnis der Tagesschwankungen des Blutdrucks bei der Hypertonie, Med. Klin. **17**: 776 (June 26) 1921.

2. Kylin, Eskil: Studien über die Tagesvariationen des arteriellen Blutdrucks bei der Hypertonie auf der Basis von Morbus Brightii, nebst einigen Bemerkungen über die Hypertoniefrage, Zentralbl. f. inn. Med. **42**: 417 (May 28) 1921.

3. Fahrenkamp, Karl: Die psycho-physischen Wechselwirkungen bei den Hypertonieerkrankungen, Stuttgart, Hippokrates, 1926.

4. Palmer, R. S.: The Significance of Essential Hypertension in Young Male Adults, J. A. M. A. **94**: 694 (March 8) 1930. Ayman, David: Normal Blood Pressure in Essential Hypertension, ibid. **94**: 1214 (April 19) 1930. Diehl, H. S., and Hesdorffer, M. B.: Changes in Blood Pressure in Young Men over a Seven Year Period, Arch. Int. Med. **52**: 948 (Dec.) 1933. MacKenzie, L. F., and Shepherd, P.: The Significance of Past Hypertension in Applicants Later Presenting Normal Average Blood Pressures, Proc. A. Life Insur. M. Dir. America **24**: 157, 1937. Robinson, S. C., and Brucer, Marshall: Range of Normal Blood Pressure: A Statistical and Clinical Study of 11,383 Persons, Arch. Int. Med. **64**: 409 (Sept.) 1939. Hines, E. A., Jr.: Range of Normal Blood Pressure and Subsequent Development of Hypertension: A Follow-Up Study of 1,522 Patients, J. A. M. A. **115**: 271 (July 27) 1940. Hines and Brown.[6]

5. Fenn, G. K.; Kerr, W. J.; Levy, R. L.; Stroud, W. D., and White, P. D.: Reexamination of 4,994 Men Rejected for General Military Service Because of the Diagnosis of Cardiovascular Defects: Individual Reports by the Chairmen of Special Medical Advisory Boards in Five Cities in Which the Combined Study Was Made, Am. Heart J. **27**: 435 (April) 1944.

6. Hillman, C. C.; Levy, R. L.; Stroud, W. D., and White, P. D.: Studies of Blood Pressure in Army Officers: Observations Based on Analysis of the Medical Records of 22,741 Officers of the United States Army, J. A. M. A. **125**: 699 (July 8) 1944.

demonstrate the influence of transient hypertension on the subsequent state of health and the cause of death, it was necessary to select, for correlation, certain specific indexes. Those chosen for the purpose were the later development of sustained hypertension and the disability retirement and death rates for cardiovascular-renal diseases.

RESULTS

First Occurrence of Transient Hypertension, by Age (table 1).—In this table are included only cases observed throughout each five year period. Those entering the study or dropping out during a given period were eliminated because it was impossible to know whether they had developed transient hypertension during those five years. There are two noteworthy features of this table—first, that transient hypertension appears not uncommonly in the younger groups and, second, that the frequency with which it is first noted

TABLE 1.—*First Occurrence of Transient Hypertension, by Age*

Age	Number Under Observation Throughout Each Age Period	Number Showing First Transient Hypertension	Frequency, per Cent
25-29	3,020	178	5.9
30-34	4,409	396	9.0
35-39	5,573	577	10.4
40-44	5,150	654	12.7
45-49	3,478	562	16.2
50-54	2,101	392	18.6
55-59	987	183	18.5

TABLE 2.—*Later Occurrence of Sustained Hypertension, by Age, in Those With and Without Transient Hypertension*

Age	Person-Years Observed: With Transient Hypertension	Person-Years Observed: Without Transient Hypertension	Number Developing Sustained Hypertension: With Transient Hypertension	Number Developing Sustained Hypertension: Without Transient Hypertension	Rate per Thousand: With Transient Hypertension	Rate per Thousand: Without Transient Hypertension	Ratio
25-29	2,127	31,072	5	14	2.4	0.5	4.8
30-34	4,401	34,670	11	30	2.5	0.9	2.8
35-39	7,261	35,218	41	59	5.6	1.7	3.3
40-44	9,709	31,501	110	81	11.2	2.6	4.3
45-49	10,386	23,705	229	126	22.0	5.7	3.8
50-54	8,218	13,736	273	133	33.2	9.7	3.4
55-59	5,268	6,508	253	97	48.0	14.9	3.2

increases with age. The curve of increase is a smooth one, beginning with 5.9 per cent in the age group 25 to 29 and reaching a plateau of 18.6 per cent at 50 to 54.

In this table and in the tables which follow, no figures are given for men under 25 years of age. This is due to the fact that no provision was made, in the statistical forms, for five year periods below this age. Such division was omitted because it was believed that a sufficient number had not been observed long enough to contribute any appreciable period of exposure. It seems likely, however, that the figures applying to the age period 25 to 29 apply also to those under age 25. Thus, 8,252 men were observed at some time prior to age 25; the total group observed at some time between ages 25 and 29 was 10,123. In both groups the frequency of transient hypertension was approximately 4 per cent. Although the inference made is not based on proper statistical procedure, in that it disregards the length of the period of observation, it probably approximates the fact. No observations were included beyond age 60 because adequate follow-up of these older men was possible in so few instances. This obtains also in the other tables.

The Later Occurrence of Sustained Hypertension, by Age, in Those With and Without Transient Hypertension (table 2).—In this and in subsequent tables the rates quoted are based on person-years observed. This method is employed to measure the total number of

TABLE 3.—*Disability Retirement Rate With Cardiovascular-Renal Diseases, by Age, for Those With and Without Transient Hypertension*

Age	Person-Years Observed *: With Transient Hypertension	Person-Years Observed *: Without Transient Hypertension	Retirements with Cardiovascular-Renal Diseases: With Transient Hypertension	Retirements with Cardiovascular-Renal Diseases: Without Transient Hypertension	Rate per Thousand: With Transient Hypertension	Rate per Thousand: Without Transient Hypertension	Ratio
25-29	2,138	31,103	0	5	0.0	0.2	0.0
30-34	4,424	34,752	3	8	0.7	0.2	3.5
35-39	7,356	35,391	14	18	1.9	0.5	3.8
40-44	10,073	31,819	52	44	5.2	1.4	3.7
45-49	10,964	24,216	98	95	8.9	3.9	2.3
50-54	8,989	14,339	184	148	20.5	10.3	2.0
55-59	6,041	6,981	230	157	38.1	22.5	1.7

* This distribution of person-years also constitutes the base for the rates in tables 4, 5 and 6.

years that all of the cases in each age group were exposed to the indicated risk. Some of the men will have been present throughout the given age period. Others will have come in during it, while still others may have dropped out before its end, either because they left the service, retired or died. Each of these individuals must be credited with the proper amount of exposure during that age period for the purpose of computing rates on the usual annual basis.

It is at once apparent that, at all ages, sustained hypertension develops more frequently in those who have previously shown transient hypertension than in those who have not. The differences in each age group are significant. The rate per thousand persons per year, i. e. per thousand person-years, increases progressively in both groups, with the ratio varying from 2.8 to 4.8.

Disability Retirement Rate with Cardiovascular-Renal Diseases, by Age, for Those With and Without Transient Hypertension (table 3).—The disability retirement rate is one index of the usefulness of an

TABLE 4.—*Disability Retirement Rate Excluding Cardiovascular-Renal Diseases, by Age, for Those With and Without Transient Hypertension*

Age	Disability Retirements Excluding Cardiovascular-Renal Diseases: With Transient Hypertension	Disability Retirements Excluding Cardiovascular-Renal Diseases: Without Transient Hypertension	Rate per Thousand: With Transient Hypertension	Rate per Thousand: Without Transient Hypertension	Ratio
25-29	4	61	1.9	2.0	1.0
30-34	18	114	4.1	3.3	1.2
35-39	42	154	5.7	3.8	1.5
40-44	75	174	7.4	5.5	1.3
45-49	78	169	7.1	7.0	1.0
50-54	80	117	8.9	8.2	1.1
55-59	48	72	7.9	10.3	0.8

officer to the Army. The figures under age 35 are not significant because of the small numbers involved. From 35 to 60 the retirement rate for cardiovascular-renal diseases is consistently greater among those with transient hypertension than in those without, and the difference in every age group above 35 is statistically significant. As the ages increase, the ratio becomes smaller. This might have been anticipated, since the

incidence of degenerative diseases increases in all persons in the older age groups, regardless of other factors. Reed and Love [7] in their biometric studies of army officers noted that cardiovascular-renal diseases developing in later life were the most frequent causes of disability and death. Of officers who were active at age 46, 11.4 per cent subsequently had a disease of this type.

Disability Retirement Rate Excluding Cardiovascular-Renal Diseases, by Age, for Those With and Without Transient Hypertension (table 4).—The ratios in this table approximate unity, although there is a slight preponderance in favor of cases of transient hypertension. However, neither the individual differences nor the series of differences as a whole show clear statistical significance.

Many persons with a permanent elevation of blood pressure give a history of vasomotor and nervous instability earlier in life.[8] In view of this fact it was thought worth while to determine the retirement rates with neuropsychiatric disorders in those with and without transient hypertension. Whereas a comparison of these rates shows a ratio favoring the group with transient hypertension consistently up to age 50, the differences are not great and, considered individually or as a whole, are not statistically significant. Redetermination of the retirement rates, excluding both cardiovascular-renal and neuropsychiatric diseases, shows them to be approximately the same in the two groups; and, again, the differences are of no statistical significance.

Death Rate with Cardiovascular-Renal Diseases, by Age, for Those With and Without Transient Hypertension (table 5).—The figures under age 35 are not significant because of the small numbers involved. From then on the death rate is consistently greater for those with transient hypertension, with rising figures in the older age groups. In fact, the difference at every age over 35 is statistically significant.

TABLE 5.—*Death Rate with Cardiovascular-Renal Diseases, by Age, for Those With and Without Transient Hypertension*

Age	Deaths with Cardiovascular-Renal Diseases: With Transient Hypertension	Deaths with Cardiovascular-Renal Diseases: Without Transient Hypertension	Rate per Thousand: With Transient Hypertension	Rate per Thousand: Without Transient Hypertension	Ratio
25-29	0	7	0.0	0.2	0.0
30-34	1	3	0.2	0.1	2.0
35-39	9	5	1.2	0.1	12.0
40-44	16	12	1.6	0.4	4.0
45-49	27	30	2.5	1.2	2.1
50-54	44	39	4.9	2.1	2.3
55-59	54	36	8.9	5.2	1.7

TABLE 6.—*Death Rate Excluding Cardiovascular-Renal Diseases, by Age, for Those With and Without Transient Hypertension*

Age	Deaths Excluding Cardiovascular-Renal Diseases: With Transient Hypertension	Deaths Excluding Cardiovascular-Renal Diseases: Without Transient Hypertension	Rate per Thousand: With Transient Hypertension	Rate per Thousand: Without Transient Hypertension	Ratio
25-29	5	176	2.3	5.7	0.4
30-34	19	131	4.3	3.8	1.1
35-39	44	104	6.0	2.9	2.1
40-44	39	89	3.9	2.8	1.4
45-49	46	74	4.2	3.1	1.4
50-54	43	52	4.8	3.6	1.3
55-59	33	37	5.5	5.3	1.0

TABLE 7.—*Survivals, Deaths and Retirements by Age 60 Among 10,000 at Age 25, According to the Death and Retirement Rates Among Officers With and Without Transient Hypertension Respectively*

	Survivals	Deaths: With Cardiovascular-Renal Diseases	Deaths: Other Causes	Deaths: Total	Retirements: With Cardiovascular-Renal Diseases	Retirements: Other Causes	Retirements: Total
With transient hypertension	4,292	609	1,202	1,811	2,289	1,608	3,897
Without transient hypertension	5,608	329	1,138	1,467	1,352	1,573	2,925
Ratio	0.77	1.85	1.06	1.23	1.69	1.02	1.33

Death Rate Excluding Cardiovascular-Renal Diseases, by Age, for Those With and Without Transient Hypertension (table 6).—As in the figures for disability retirement, the death rate is slightly higher in the group with transient hypertension. The ratios are not as large, however, as in the death rates for cardiovascular-renal diseases. Although only one of the individual differences is statistically significant (that for the 35 to 39 age group), there is significance in the series of differences as a whole. If, in addition to cardiovascular-renal diseases, neuropsychiatric disorders and suicide are excluded as a cause of death, the rate remains slightly higher in the group with transient hypertension. The series of differences is still significant although much less so than before this exclusion. The reason for these differences is not evident.

The death rate with neuropsychiatric disorders after age 30 is uniformly and significantly higher in the group with transient hypertension. It should be stressed, however, that almost all of these deaths were due to suicide.

Summarized, Cumulative Actuarial Tables.—In tables 7 and 8 the figures have been recast in actuarial form. In table 7 are given survivals, deaths and retirements by age 60 among 10,000 officers of age 25, according to the death and retirement rates, with and without transient hypertension. At the end of such an observation period there would be 4,292 survivors with a record of transient hypertension, contrasted with 5,608 without it—a ratio of 0.77. Among those who died of cardiovascular-renal diseases, 609 would have had transient hypertension and 329 would not—a ratio of 1.85. Deaths from other causes among those with

TABLE 8.—*Survivals and Deaths by Age 60 Among 10,000 at Age 25, According to the Death Rates Among Officers With and Without Transient Hypertension Respectively*

	Survivals	Deaths: With Cardiovascular-Renal Diseases	Deaths: Other Causes	Deaths: Total
With transient hypertension	7,777	823	1,400	2,223
Without transient hypertension	8,333	410	1,257	1,667
Ratio	0.93	2.01	1.11	1.33

7. Reed, L. J., and Love, A. G.: Biometric Studies on Army Officers—Somatological Norms in Disease, Human Biol. **5**: 61 (Feb.) 1933.

8. O'Hare, J. P.; Walker, W. G., and Vickers, M. C.: Heredity and Hypertension, J. A. M. A. **83**: 27 (July 5) 1924.

transient hypertension would have been 1,202, as against 1,138 among those without—a ratio of 1.06.

With respect to retirements for disability with cardiovascular-renal diseases, there would have been 2,289 in the group with transient hypertension and 1,352 without—a ratio of 1.69. Retirement for other causes would have occurred 1,608 times in the group with transient hypertension and 1,573 in the group without—a ratio of 1.02.

In table 8 appear the survivals and deaths by age 60, among 10,000 officers at age 25, with and without transient hypertension, according to the death rates only. At age 60 there would be 7,777 survivals among those with transient hypertension and 8,333 without—a ratio of 0.93. Deaths from cardiovascular-renal diseases for those with transient hypertension would number 823, as against 410 for those without—a ratio of 2.01. Deaths from other causes would number 1,400 in those with transient hypertension and 1,257 in those without—a ratio of 1.11. These tables bring into focus, in condensed form, the higher rates of disability retirement and death in the group with transient hypertension.

COMMENT

The upper limits of the normal blood pressure have not been firmly established. The critical levels of 150/90 used in this study are those prescribed in Mobilization Regulations 1-9, issued by the War Department on Oct. 15, 1942. The standards of physical examination for commission in the Regular Army, according to Army Regulations 40-105, define hypertension as a persistent systolic blood pressure of 150 or more or a persistent diastolic of 95 or more if the candidate is over 25 years of age, and a persistent systolic of 140 or more or a persistent diastolic of 90 or more if the candidate is less than 25 years of age. It has seemed proper to accept 150 systolic and 90 diastolic as the upper limits in this study because of the large numbers now involved in Selective Service examinations. The relative importance of various higher levels, both systolic and diastolic, will be considered in a forthcoming publication.

No mention has been made of the condition of the retinal vessels. Records concerning them were available in so few cases that no conclusions are justified. The cold pressor test [9] was not employed in any of these examinations, but hyperreaction to cold and to emotion appear to carry similar implications.

Two recent papers have appeared dealing with the problem of transient hypertension in the Navy. Master [10] called back for reexamination 50 patients, all 40 years of age and over, who during their stay in the hospital one to seven years previously had shown blood pressure readings at the upper limits of normal. These varied from 140 to 156 systolic and 80 to 94 diastolic. There was only a single reading for each patient. On reexamination, 76 per cent were found with hypertension and at least 25 per cent had a diastolic pressure over 100. It was concluded that even one high reading may be an indication of future hypertension and that some men with such levels may already have cardiovascular disease. The suggestion was made that in borderline cases a complete physical examination should be performed and the final decision should be based on the composite picture presented.

A somewhat more liberal point of view has been expressed by Rogers and Palmer.[11] During one month at the Office of Naval Officer Procurement, Boston, they found that 222 of 1,574 applicants (14 per cent) had mild variable hypertension at the initial examination. Their recommendations, however, are based on a favorable follow-up experience, in civilian life, with 25 cases of nervous hypertension and 448 cases of early and late essential hypertension. They suggest criteria for the acceptance of applicants who show a labile blood pressure and conclude that transient nervous hypertension, taken as the first sign of essential hypertension, need not be disqualifying for military service.

The results of the present study must be applied according to the need for men in the armed forces. It is clear that persons who show a transient elevation of blood pressure above 150 systolic or above 90 diastolic are more likely to show sustained hypertension at a later date than those whose readings remain below these levels. In addition, the transient hypertension group shows higher rates for disability retirement and death from some form of cardiovascular-renal disease than does the group with a consistently normal blood pressure. It is also apparent that in those with transient hypertension there are slightly higher death rates from diseases other than those affecting the cardiovascular system and kidneys. This is explained in part, though not entirely, by the higher mortality, in this group, from nervous and mental diseases, and particularly from suicide. The same general trend is evident in the retirement rates, although here the differences are not clearly significant.

SUMMARY AND CONCLUSIONS

1. An analysis has been made of the medical records of 22,741 officers of the United States Army in order to appraise the significance of transient hypertension. Blood pressure readings over 150 mm. of mercury systolic or over 90 diastolic were considered abnormally high.

2. The length of the observation period was from one year to more than twenty-five years; 84 per cent were under observation from five to nineteen years and 38 per cent from fifteen to nineteen years. In 1,437 instances the duration of the observation period was twenty years or over. These figures are quoted from the first paper in the series.[6]

3. The frequency with which transient hypertension was first noted increased with age. The curve of increase was smooth, beginning with 5.9 per cent in the age group 25 to 29 and reaching a plateau of 18.6 per cent at 50 to 54.

4. At all ages, sustained hypertension developed more frequently in those with previous transient hypertension than in those who never showed an elevation of blood pressure. In both groups the rate increased with advancing years.

5. The rate for disability retirement with cardiovascular-renal diseases, which is one index of the usefulness of an officer to the Army, was consistently higher among those with transient hypertension than in those without, at all ages from 35 to 60.

6. The death rate with cardiovascular-renal diseases was also higher in those with transient hypertension; the figures rose in the older age groups.

7. Both disability retirement and death rates from diseases other than those of cardiovascular-renal origin

9. Hines, E. A., Jr., and Brown, G. E.: A Standard Test for Measuring the Variability of Blood Pressure: Its Significance as an Index of the Prehypertensive State, Ann. Int. Med. **7**: 209 (Aug.) 1933.

10. Master, A. M.: Cardiovascular Problems in the War: Hypertension and the Navy, Bull. New York Acad. Med. **19**: 704 (Oct.) 1943.

11. Rogers, W. F., and Palmer, R. S.: Transient Nervous Hypertension as a Military Risk: Its Relation to Essential Hypertension, New England J. Med. **230**: 39 (Jan. 13) 1944.

were slightly higher in the group with transient hypertension. In the case of the retirement rates the differences were not significant. The higher death rates in the group with transient hypertension were explained in part, though not entirely, by the relatively greater number of suicides.

8. The decision as to the usefulness to the Army of a man with transient hypertension will depend on the need for manpower. If this is urgent he may be accepted, provided heart, arteries and kidneys are normal. In doubtful cases the examination should include a teleroentgenogram of the heart and an electrocardiogram, as well as examination of the retinal vessels and urine. A certain number so accepted will develop permanent hypertension and the number will increase as age advances; in this series the rate per thousand ranged from 5.6 between the ages of 35 and 39 to 48.0 between 55 and 59. During times of peace, or whenever the need for men in the service is not acute, the transient hypertensive is not to be regarded as a first rate risk; he may later prove a burden to the Veterans Administration.

9. It seems probable that the facts pertaining to transient hypertension which have been derived from an analysis of the records of army officers apply also to the general male population of comparable physical fitness and similar age groups.

ABSTRACT OF DISCUSSION

DR. E. A. HINES JR., Rochester, Minn.: It is often stated in articles in medical textbooks and periodicals that transient elevations of blood pressure are due to nervous tension and therefore are of no significance. It is usually further advised that subsequent blood pressure readings should be taken when the subject is more relaxed and that the lowest reading should be recorded as the proper blood pressure reading. The proponents of the idea that such elevations of blood pressure are of no significance have offered no proof that this is so. As Dr. Levy has indicated, there are those who believe that transient elevations of the blood pressure, particularly in the diastolic blood pressure, may be indicative of a prehypertensive state, if not actually representative of the earliest stages of hypertensive disease. The data which Dr. Levy and his associates have presented are another link in the chain of evidence supporting this contention. Dr. Levy has concluded that transient elevations of blood pressure are probably of some significance in the subsequent development of hypertension. He has not been able to state or to show just what should be done with the individual with an elevation of blood pressure which sometimes goes into the upper range of normal. For instance, what should be done with a person 20 years of age who has a blood pressure of 150 systolic and 95 diastolic, or what should be done with a person of 30 who has a blood pressure of 145 systolic and 90 diastolic? The answer to this question—and it is a most pertinent one—probably cannot be obtained as far as concerns the armed services without a long term follow-up study of a group of young men and women which is sufficiently varied and adequately controlled and who have had special blood pressure studies carried out and have been followed in the armed services through varying types of duties and for from ten to twenty years afterward.

DR. ROY W. SCOTT, Cleveland: Both the large number (22,741) and the length of time over which the observations of Dr. Levy and his colleagues extended make this study of great statistical value. Clinicians may now speak with increasing assurance about certain concepts based on personal experience gained in following patients with vascular disease and hypertension. Among these is the more frequent appearance of sustained hypertension at all ages in persons with previous transient hypertension. Since transient hypertension is a frequent forerunner of sustained hypertension, which in turn is so often associated with arterial and arteriolar disease, one would expect, as these workers have found, that both the rate of disability retirement and the death rate from cardiovascular renal disease are higher in persons with transient hypertension. These data are so consistent with clinical experience among the civilian population that the facts derived from their analysis of the records of army officers probably apply to our male population of comparable physical fitness and similar age group.

DR. N. S. DAVIS III, Chicago: It seems that the syndromes characterized by arterial hypertension develop whenever the auxiliary humeral renal-hypertensin pressor mechanism becomes permanently established. This occurs when "emotional" hypertension or that caused by fatigue, overexertion or exposure to cold or high altitude is of sufficient duration to exhaust the adrenals and prevent the secretion of adequate amounts of epinephrine, when there is hypoadrenalism with the formation of toxic steroids which inhibit renal amino acid oxidation, when adrenal corticosterones are increased sufficiently to inhibit renal amino acid oxidation, when there is renal ischemia due to vasoconstriction of anomalous arteries or when the formation or action of renal amino acid oxidases is inhibited because of exposure to toxic chemicals, to toxic metabolic and bacterial products of disease or because of deficient intake, absorption and utilization of minerals, amino acids and vitamins required for their synthesis. When renal oxidation is inhibited, deamination of amino acids is by decarboxylation with the formation of pressor amines, which cause local foci of renal ischemia and the formation of renin. The renin reacts with the alpha globulin hypertensinogen to form hypertensin, which causes more renal vasoconstriction and so increases renin formation. Thus the renin-hypertensin pressor mechanism tends to establish itself and initiate the insidiously progressive syndrome with which high arterial tension is associated.

DR. ROBERT L. LEVY, New York: Although, as a group, those showing a transient elevation of blood pressure are more likely later to develop sustained hypertension and various manifestations of cardiovascular-renal disease, this sequence of events is by no means invariably observed. Our next problem is to define, if possible, adequate criteria for the recognition of those persons in whom transient hypertension is an early sign of future trouble.

Clinical Notes, Suggestions and New Instruments

SULFADIAZINE SENSITIVITY

THE CAUSE OF SEVERE TOXIC SYMPTOMS IN A CHILD

PHYLLIS KOTEEN, M.D., NEW YORK

This case is reported because of severe and unusual manifestations of sulfadiazine idiosyncrasy and diagnostic and therapeutic problems involved.

P. R.,[1] a white boy aged 5½ years, was admitted to the private pediatric service of the New York Hospital on Feb. 24, 1944 with the chief complaints of fever and cough of four days' duration.

Two years prior to admission the patient suffered from otitis media and mastoiditis, for which he was treated at another hospital with sulfadiazine and sulfathiazole. His mother believed that hematuria had occurred with sulfadiazine therapy, and fever and a rash with sulfathiazole. Following this illness the patient remained well except for respiratory infections until the onset of the present illness.

The present illness began February 6, eighteen days before admission, with fever and sore throat, which improved without specific therapy. Ten days prior to admission a sibling had a streptococcic sore throat and rash. On February 18 the patient vomited, complained of slight abdominal pain and had three loose bowel movements. The following day he started to cough. Two days later sulfadiazine therapy was begun because of a temperature of 39 C. (102.2 F.), signs of a severe respiratory infection and tonsillitis. He received 0.75 Gm. every four hours for a total dosage of 9 Gm. Absence of

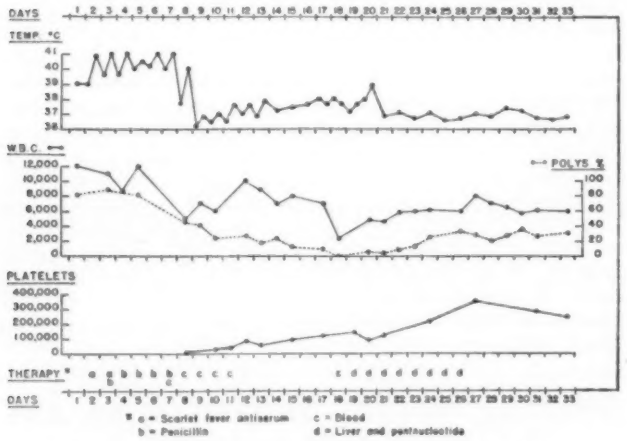
From the Department of Pediatrics of the New York Hospital and Cornell University School of Medicine.

1. Dr. Benjamin Spock gave me permission to report this case.

response led to discontinuance of the drug, and on the following day he was admitted to the hospital.

On admission, examination revealed that the patient was moderately well developed, slender, flushed and listless, but he did not appear severely ill. His temperature was 39 C. rectally. The skin was dry and showed a fine brawny desquamation; at the left wrist were a few pink maculopapular lesions. The nasal turbinates were inflamed; the tongue was coated and dry. The tonsils were hypertrophied and injected. Examination of the chest revealed increased tactile fremitus, exaggerated breath sounds and rhonchi throughout the right side. The abdomen was diffusely tender; the spleen was firm and was palpated 2.5 cm. below the costal margin; the liver was felt 1 cm. below the costal margin in the midclavicular line. The remainder of the examination was negative.

On admission the hemoglobin was 11 Gm., the red blood cells were 4.4 million and the white blood cells were 12,000, with a differential of 17 per cent lymphocytes and 83 per cent polymorphonuclear leukocytes. On smear no abnormal blood cells were noted, and the platelets appeared adequate. The urine was clear and yellow, with a specific gravity of 1.025 and without albumin, sugar, red cells, white cells or casts. Subsequent urine examinations, red cell counts and hemoglobin



Temperature chart, therapy and essential laboratory data.

determinations remained normal. The changes in leukocyte count, differential and platelets are recorded in the accompanying chart. Daily blood cultures taken for the first five days showed no growth. Initial throat cultures grew a few beta hemolytic streptococci and Hemophilus influenzae. Repeated blood agglutinations for the typhoid-paratyphoid group, Brucella, rickettsial organisms and heterophile antigen were negative. X-ray examination of the chest gave normal results.

On the second hospital day the patient's temperature reached 40.8 C. (105.4 F.), his tonsils appeared more injected and the cervical glands seemed larger. On the assumption that this infection was caused by the beta hemolytic streptococcus, 100 cc. of anti-scarlet fever convalescent serum was administered. The following day this high fever was maintained, and the patient appeared very toxic and developed a diffuse morbilliform rash. An additional 100 cc. of convalescent serum was given without effect. Because of the questionable history of sulfonamide sensitivity these drugs were not used.

Despite the report of no growth in the first blood culture, septicemia appeared the most likely diagnosis. For this reason penicillin therapy was started on the third hospital day. He received a total of 500,000 units in the subsequent four days. During this interval the throat infection and cervical lymphadenitis subsided entirely; however, the patient's condition became critical, he was semicomatose and generalized edema developed. The temperature ranged from 39 to 41 C. (102.2 to 105.8 F.), the rash became more extensive and numerous petechiae appeared. It was apparent that penicillin was not influencing the general course of the disease, and many unusual febrile illnesses were considered as a possible cause of this boy's serious condition. On the eighth hospital day it was noted that the patient's blood in a tube did not clot for thirty minutes. The prothrombin level [2] was found to be 54 per cent of normal, and the platelet count [3] was 8,000 on this day. The diagnosis of sulfadiazine sensitivity with thrombocytopenia and severe generalized toxic symptoms seemed justified. This opinion was substantiated by a sulfadiazine blood level of 2.3 mg. per hundred cubic centimeters four days after cessation of therapy and the presence of detectable amounts of the drug in the blood after twelve days.

The patient received several direct transfusions and showed gradual clinical improvement and rise in platelet count. However, on the eighteenth day the white count fell precipitously to 2,200 with complete disappearance of the granulocytes. He was given 2 cc. of liver extract and 10 cc. of pentnucleotide daily for eight days. His improvement was steady thereafter and he was discharged on the thirty-seventh hospital day, at which time his blood picture had returned to normal. He was clinically well with the exception of remaining hepatosplenomegaly.

After discharge, details of the patient's previous hospitalization became available. He had been hospitalized two years previously because of otitis media and mastoiditis. He was given sulfadiazine therapy, and ten days after initiation of this treatment he developed a rise in temperature, generalized maculopapular rash, lymphadenopathy and hepatosplenomegaly. Sulfathiazole was given a few days later because of tonsillitis. The patient responded with anuria, a hemorrhagic rash and continued hepatosplenomegaly. A reduction in the polymorphonuclear leukocytes occurred eight days after discontinuance of the sulfathiazole.

If this record had been available at the time of the patient's hospitalization there would have been no diagnostic problems. However, he would still be of interest because of the variety and severity of toxic manifestations presented by 1 patient. Hepatosplenomegaly has rarely been reported as a complication of sulfonamide therapy. Williams [4] reports 1,000 cases of infection treated with sulfapyridine. Twelve of these patients developed rashes, and 9 had concurrent hepatosplenomegaly. One case fully reported was similar to ours, with a severe toxic reaction, purpuric rash, edema, enlarged liver and spleen and basal rales. No mention was made of platelets, and there was leukocytosis with eosinophilia in contradistinction to our case.

There have been only a few instances of thrombocytopenic purpura noted resultant from all forms of sulfonamide therapy. When this complication does occur it is apt to be extremely serious.[5] Five out of 9 cases reported terminated fatally. An additional case of thrombocytopenia following three weeks of sulfadiazine therapy occurred in a boy aged 5 years in our wards.[6] He developed a picture resembling the Waterhouse-Friedrichsen syndrome, with diffuse hemorrhages into the skin, shock and a low platelet count. Autopsy revealed massive hemorrhages into the adrenals, which seemed satisfactorily accounted for by the depressed platelets and not by septicemia. These reactions appear to be definitely due to sensitivity to sulfonamides and not to direct toxic reaction of the drug on the platelets. Kracke and Townsend [7] followed 61 patients receiving sulfathiazole and found an increase in the platelet count during the course of therapy.

The other reactions exhibited by our patient, such as hyperpyrexia, rash and agranulocytosis, are of more frequent occurrence and have hitherto been reported adequately.[8]

2. Kato, K.: Micro-Prothrombin Test, Am. J. Clin. Path. **10**: 147, 1940.
3. Direct method; normal value 200,000 to 300,000.
4. Williams, H. V.: Hepatosplenomegaly with Other Clinical Reactions to Sulfapyridine, Lancet **1**: 105, 1943.
5. Hurd, R. W., and Jacox, R. F.: Thrombopenic Purpura Developing as a Complication of Sulfathiazole and Sulfadiazine Therapy, J. A. M. A. **122**: 296 (May 29) 1943. Gorham, L. W.; Propp, S.; Schwind, J. L., and Climenko, D. R.: Thrombocytopenic Purpura Caused by Sulfonamide Drugs: A Report of Three Cases, Am. J. M. Sc. **205**: 246, 1943. Kracke and Townsend.[7]
6. Dale, J., Jr.: Personal communication to the authors.
7. Kracke, R. R., and Townsend, E. W.: The Effect of Sulfonamide Drugs on the Blood Platelets: Report of Two Cases of Thrombopenic Purpura and Experimental Studies on Patients Receiving Sulfonamide Drugs, J. A. M. A. **122**: 168 (May 15) 1943.
8. Finland, M.; Peterson, O. L., and Goodwin, R. A.: Sulfadiazine: Further Clinical Studies of Its Efficacy and Toxic Effects in 460 patients, Ann. Int. Med. **17**: 920, 1942. Spink, W. W.: Sulfanilamide and Related Compounds in General Medicine, ed. 2, Chicago, Year Book Publishers, Inc., 1942.

SUMMARAY

A case of severe and unusual sulfadiazine sensitivity with multiple manifestations presented hyperpyrexia, rash, generalized edema, a semicomatose state; lymphadenopathy, hepatosplenomegaly, thrombocytopenic purpura and agranulocytosis, with eventual recovery.

New York Hospital.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

ALLERGENIC EXTRACTS (See New and Nonofficial Remedies, 1944, p. 35).

ENDO PRODUCTS, INC., RICHMOND HILL, N. Y.

Allergenic Extracts: The following extract is marketed in treatment set packages of four 10 cc. vials containing, respectively, slightly more than 1 cc. of a 2.5 per cent, 0.25 per cent, 0.025 per cent and 0.0025 per cent dilution of the original extract in glycerosaline solution (50 per cent glycerin) and four 10 cc. vials containing 9 cc. of diluting fluid (0.4 per cent phenol in isotonic solution of sodium chloride). The extract is also supplied in special treatment packages of one 10 cc. vial containing 4 cc. of a 2.5 per cent dilution of the original extract in glycerosaline solution (50 per cent glycerin) and one 10 cc. vial containing 6 cc. of diluting fluid (0.4 per cent phenol in isotonic solution of sodium chloride).

House Dust (Purified Concentrate).

Allergenic extract house dust (purified concentrate)-Endo is prepared from dust obtained from mattresses and household furniture.

A mixture of 1 part by weight of house dust and 2 parts by volume of distilled water is covered with toluene and extracted while stirring, at 0 to 5 C. for seventy-two hours. The aqueous extract is separated from the dust by centrifugation.

Three volumes of the water extract are cooled to 0 to 5 C. and treated with 2 volumes of previously cooled acetone. The precipitated material, separated by centrifugation, is discarded. Acetone is added to the clear centrifugate until a concentration of 75 per cent acetone is reached. The precipitated material is centrifuged and the liquid is discarded. Adhering acetone is blown off with cold dry air. The precipitate is taken up in one tenth the original volume of distilled water. Three volumes of this aqueous solution are treated with 2 volumes of acetone, mixed thoroughly and centrifuged. The liquid is reserved. The residue is washed with a small amount of a 40 to 60 per cent V/V acetone-water solution until the original volume of supernatant and wash liquids is equal to one tenth the original volume. Sufficient acetone is added to yield a 75 per cent concentration. The syrupy precipitate is separated by centrifugation and the adhering acetone is removed by cold dry air. The syrup is taken up with one tenth the original volume of distilled water and dialyzed against running distilled water until about 50 per cent of the total dissolved solids has been removed. To the 5 per cent solution w/v (adjusted by low temperature vacuum distillation if necessary), obtained by dialysis, sodium chloride is added (1.8 Gm. per hundred cubic centimeters) and the solution is passed through a Seitz filter. The sterile solution is added to an equal volume of previously sterilized glycerin. This solution of 2.5 per cent allergenic extract constitutes the stock solution from which appropriate dilutions are prepared. All diluted solutions are passed through a Seitz filter before filling into sterile vials by aseptic technic.

Allergenic Extracts Diagnostic: The following extract is marketed in packages of a single vial, with accompanying applicator containing 1 cc. of a 1:200 solution (0.5 per cent) of the original extract in 50 per cent glycerin.

House Dust (Purified) Concentrate.

This extract, for use by the scratch method and cutaneous testing, is prepared in much the same manner as the allergenic extract-Endo, for treatment, just described. The procedure is the same up to the point of dialysis, whereupon the extract for diagnosis undergoes the following treatment: To the solution obtained immediately before dialysis ammonium sulfate is added (60 Gm. per hundred cubic centimeters). The coagulated material is centrifuged. The separated solid is dissolved in one-half the original volume of distilled water and the ammonium sulfate precipitation is repeated. The solid separated by centrifugation is suspended in a small volume of water and dialyzed until the solution in the sac does not respond to tests for the sulfate ion. The dialyzed solution is centrifuged to remove a small amount of suspended solids and the solution is adjusted (by vacuum distillation at low temperature if necessary) to contain 1 per cent of dissolved solids. Sufficient sodium chloride is added to yield a 1.8 per cent solution with respect to sodium chloride. The solution is diluted with an equal volume of glycerin and filtered through a Seitz filter. This 0.5 per cent solution constitutes the allergenic extract purified house dust concentrate for diagnosis by scratch testing.

Council on Physical Medicine

The Council on Physical Medicine has authorized publication of the following article. HOWARD A. CARTER, *Secretary.*

ARTIFICIAL RESPIRATION—MANUAL AND MECHANICAL

In all cases of asphyxia it is of paramount importance that artificial respiration be administered immediately. Loss of a minute may mean the difference between life and death. There is little hope of reviving a victim who has ceased to breathe for more than five to seven minutes and even less chance if he has been in a state of apnea for more than ten minutes. Effective artificial respiration may be applied by the acceptable manual methods—Schafer prone pressure and Howard-Silvester methods—or by mechanical means—respirator or resuscitator. The inhalator is a valuable adjunct to manual methods of artificial respiration. One disadvantage to mechanical apparatus, either resuscitator or inhalator, is that it is not always on the scene of an accident and precious first minutes or seconds may be lost waiting for its arrival.

All rescue crews, and also the public, should be taught a correct method of administering manual artificial respiration. The one most generally used is the Schafer prone pressure method, which may be administered effectively by one person. The American Red Cross, the Boy Scouts and the Y. M. C. A. give instruction in this method. Physiologic experiments prove that an exchange of air in the lungs is achieved when the method is applied correctly. The Council highly recommends that every man, woman and child take advantage of the opportunity made available through defense activities to learn how to apply manual artificial respiration.

The Howard-Silvester method is somewhat more cumbersome to administer and requires the services of a team of trained persons. The Coast Guard uses this method.

In 1932 Dr. F. C. Eve of Hull, England, described a new method of artificial respiration which is unlike all previous methods mentioned. It is a rocking method, and the force of gravity causes the abdominal organs to shift, thus moving the diaphragm in and out like a bellows. It has been adopted on the British warships. In Eve's method the drowning victim is laid face downward on a stretcher and is well wrapped with blankets. His wrists and ankles are lashed to the handles. Then he is hoisted on a trestle or sling and rocking is begun. This method, according to Dr. Eve, is best because in cases of drowning the inspiratory recoil may be lost as the result of loss of tone in the diaphragm, and it is independent of tone. This method is safe and can be done by any one, but the disadvantage is that the equipment, although simple, may not be on hand in emergency cases when it is needed.

Included in the Council's list of accepted devices are inhalators and resuscitators, the two types of apparatus for administering mechanical artificial respiration. These devices are often confused as to function; the following briefly describes them:

Inhalators provide an atmosphere of oxygen and carbon dioxide gas mixture slightly higher than atmospheric pressure around the mouth and nose of the victim and are used in conjunction with an approved method of manual artificial respiration. Inhalators consist essentially of a face piece, rubberized fabric breathing bag, pressure reducing valve, tanks of carbon dioxide-oxygen mixture and carrying case.

Resuscitators create positive and negative pressure by means of a mechanical appliance operated by the energy of the stored gas merely positive pressure only. A face piece, reduction valve, tanks of carbon dioxide-oxygen mixture or merely tanks of oxygen, a carrying case and a reciprocating mechanism are the principal parts of the resuscitator.

The efficacy of the two types of appliances has been shown to be essentially the same by the evidence coming to the Council. Records show that when an inhalator and a resuscitator are on the scene of an accident at the same moment, and if either one is employed efficiently, the final result will not differ.

The Council on Physical Medicine is now carrying on a five year survey and is supporting research on artificial respiration. It is hoped that this work will produce additional data.

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SATURDAY, NOVEMBER 25, 1944

ENVIRONMENTAL CANCER

Environmental cancer is cancer due to prolonged contact with some cancerigenic agent in the environment. The relationship of a previous exposure to such an agent and the cancer often appearing many years later is frequently overlooked or not understood. Environmental cancers can be divided into four main groups according to the type of exposure:

First are the cancers caused by agents in the normal environment. Representative of this group is cancer due to the continued ingestion of arsenic in drinking water and foodstuffs in certain regions, the solar cancers of the skin in dry and sunny regions, as in our Midwestern and Southwestern states, the bladder cancers in people in places like Egypt with endemic schistosomiasis, and possibly also lung cancers due to inhalation of road dust containing cancerigenic tar. The second group of environmental cancer results from certain habits (habitual cancer), as for example cancer of the lip and mouth in smokers, cancer of the oral lining in betel and tobacco chewers, and cancer of the abdominal skin in kangri users. The third group comprises cancer resulting from use of certain medicinal agents (medicinal cancers), e. g. cancer of the skin after arsenical medication and after exposure to roentgen rays and radioactive substances. The fourth, which is the largest and most important group, is represented by occupational cancer elicited by exposure to chemical and physical agents in the course of regular occupations.[1]

The agents known or suspected to cause occupational cancer are arsenic, chromates, nickel carbonyl, radium, mesothorium, asbestos, crude and processed mineral oils, pitch, tar, soot, paraffin oil, anthracene oil, creosote, aromatic amino compounds (aniline, naphthylamine, benzidine), benzene, ultraviolet rays, roentgen rays, radioactive materials and substances from certain parasitic worms. Approximately 8,000 to 9,000 cases of occupational cancer appear to have been placed on record, the majority during the last two to three decades, during which the sources of occupational cancer were mostly discovered. These figures, however, do not reflect the actual incidence of industrial cancer, as the cause of many cases of this type is not properly recognized or their occurrence is not recorded.

Environmental cancer may involve many organs and tissues, notably the skin, lip, tongue, cheek, oral cavity, nasal sinuses, larynx, bronchi, lung, liver, kidney, ureter, bladder, connective tissue, bone and hemopoietic tissues. The site of the cancer depends on the type of the cancerigenic agent and the kind of exposure. The sex ratio is determined mainly by the exposure to the various cancerigenic agents. It is for this reason that the male sex is predominantly affected by occupational cancer, but osteogenic sarcoma occurs in women working in luminous dial factories. Undoubtedly the rapid increase in the employment of women in hazardous industries will be followed by an increase of occupational cancer in women.

The public health importance of industrial cancer undoubtedly will increase not only with respect to the number of workers, male and female, exposed to industrial cancerigenic agents but also with respect to the variety of plants and operations in question. Public health authorities will wish to institute effective technical and sanitary supervision of such establishments as well as medical control of the workers, present as well as past. Practitioners and cancer clinics, in addition to industrial physicians, will aid greatly in meeting this situation by close study of the occupational history of all patients coming to them with precancerous and cancerous lesions. It is mainly in this way that the industrial origin of cancer can be established and new sources of occupational forms discovered. The benefits from such efforts will be not only the early detection and improved prognosis of cases of occupational cancer but also the prevention of industrial cancer by the elimination of exposures to cancerigenic agents. Industrial cancer is largely preventable by proper technical measures.

Organized investigation of environmental and especially occupational cancers is a promising approach to the study of fundamental problems of human cancer because these cancers are the counterpart of experimental cancer in animals. Environmental cancers permit a scientific analysis of cancerigenic agents and of local and general reactions induced by them in human beings.

1. Clemensen, J.: Cancer and Occupation in Denmark, 1935-1939, Copenhagen, Nyt Nordisk Forlag-Arnold Busck, 1941. Davis, E.: Chemical Carcinogenesis, Drugs, Dyes, Remedies and Cosmetics with Particular Reference to Bladder Tumors, J. Urol. **49**: 14, 1943. Gross, E.: Das Carcinom vom Standpunkt des Gewerbetoxikologen, Ztschr. f. angew. Chem. **53**: 368, 1940. Hueper, W. C.: Occupational Tumors and Allied Diseases, Springfield, Ill., Charles C Thomas, 1942, p. 896; Cancer in Its Relation to Occupation and Environment, Bull. Am. Soc. Control of Cancer **25**: 6, 1943. Warren, S.: Minimal Criteria Required to Prove Causation of Traumatic or Occupational Neoplasms, Ann. Surg. **117**: 585, 1943.

TRANSITORY PULMONARY INFILTRATIONS ASSOCIATED WITH EOSINOPHILIA—LOEFFLER'S SYNDROME

Loeffler reported in 1932 and again in 1936 [1] a syndrome characterized by transitory pulmonary infiltrations, blood eosinophilia and a mild clinical course which was in striking contrast to the extensive pulmonary lesions as seen in the roentgenograms. Some of the cases were discovered in supposedly normal persons in the course of mass radiography, while others were in ambulatory cases suspected of pulmonary tuberculosis. Symptoms when present were those of fatigue, irritating cough, associated sometimes with pain in the chest and with scanty sputum; normal or moderately elevated temperature; mild leukocytosis, and increased sedimentation rate. Exaggerated vesicular breathing and sibilant rales over the area of infiltration were the only auscultatory signs. The eosinophilia ranged from 6 per cent to 66 per cent and accompanied rather than followed the appearance of the infiltration of the lung, so that it could not be considered a postinfectious phenomenon. However, strict parallelism between the extent of the infiltration and the grade of eosinophilia was not demonstrable.

The essential and distinguishing feature of the syndrome as emphasized by Loeffler is the fleeting, migratory character of the infiltrations. The shadows appear and disappear in from three to eight days. They may be extensive and irregular in shape or small and round, resembling remarkably the shadows of primary tuberculous infiltration; they may be fleecy or dense, unilateral or bilateral; they may involve the entire lung or be limited to one lobe. In a small number of cases Loeffler observed involvement of the pleura with occasionally small circumscribed pleuritic effusion. Breton [2] likewise stresses the fleeting, migratory and in some cases recurring character of the x-ray shadows in the Loeffler syndrome and points out that attacks of asthma, which, according to various authors, accompany the syndrome in from 5 to 8 per cent, need not be considered as an essential feature of the syndrome. The syndrome is observed more frequently in asthma because the latter is the most frequent allergy.

Pathologic observations on this condition are limited to postmortem studies of Meyenburg [3] on four accidental deaths. He found that the infiltrations were of pneumonic type with exudation into the alveoli and with eosinophilic infiltration of both the alveoli and the interstitial tissue. There was also an inflammatory involvement of the pleura and of the interlobar fissures. Meyenburg failed to demonstrate tubercle bacilli or Ascaris larvae in the pulmonary tissue.

The etiology of the syndrome is obscure. Loeffler first suspected that these cases represented a mild atypical form of pulmonary tuberculosis. Maier [4] reviewed the 100 cases seen at Loeffler's clinic in Zurich and found only 2 patients with active tuberculosis at the time of sickness; the tuberculous process was present in both for some time. The first important contribution to the etiology of the syndrome is probably that of Engel, who had observed seasonal occurrences of cough in Shanghai which coincided with the flowering of the privet plant. Fifty-two of the 100 cases in Maier's series displayed such allergic phenomena as eczema, hay fever, migraine, vasomotor rhinitis and urticaria either before or at the time of the illness. The blood eosinophilia of course suggested the allergic character of the disease. Swiss observers emphasized the rather frequent association of the syndrome with Ascaris infestation. Thus Zweifel [5] found sensitivity to Ascaris extract in 70 per cent of the cases with the Loeffler syndrome, whereas normal persons, persons with ascaridiasis and allergic persons reacted to it in only 40 per cent. Zweifel concludes that, while Ascaris appears to be the most frequent cause of these pulmonary infiltrations, it is not the exclusive allergen. Lavier [6] reported a case of hepatitis associated with Loeffler's syndrome caused by the liver fluke (Fasciola hepatica). Hoff and Hicks [7] reported a case in which asthmatic attacks and pulmonary infiltrations which persisted for three months disappeared dramatically on the discovery and treatment of Endameba histolytica. The syndrome appears to represent a genuine allergic phenomenon, the pulmonary tissues constituting the shock organ. Gravesen [8] stresses that it is the intersitial tissue of the lung that is hypersensitive rather than the bronchi, as is the case in asthma. The cases in which ascarids appear to be the cause raise the question whether the pulmonary infiltrations are the result of invasion of the lungs by the larvae of the helminth or whether these infiltrations represent a purely allergic inflammatory reaction in response to the Ascaris toxin. Most observers, including Maier, failed to find the larvae of the ascarids in the sputum. The only support for the thesis of this being an Ascaris larva pneumonia is the experiment of Koino, in which he swallowed 2,000 larval eggs of ascarids with resultant pneumonic consolidation and sputum containing larvae. This experiment of course is not necessarily comparable to the natural evolution of the disease.

1. Löffler, W.: Die flüchtigen Lungeninfiltrate mit Eosinophilie, Schweiz. med. Wchnschr. **66**: 1069 (Nov. 7) 1936.
2. Breton, A.: A Propos de la radiologie de l'asthme: Le syndrome de Löffler, Paris méd. **28**: 538 (June 25) 1938.
3. von Meyenburg, H.: Eosinophilic Pulmonary Infiltration: Pathologic Anatomy and Pathogenesis, Schweiz. med. Wchnschr. **72**: 809 (July 25) 1942; abstr. J. A. M. A. **121**: 626 (Feb. 20) 1943.
4. Maier, C.: Das flüchtige eosinophile Lungeninfiltrat, zusammenfassende Ergebnisse von über 100 Beobachtungen, Helvet. med. acta. **10**: 95 (April) 1943.
5. Zweitel, E.: Hautprüfungen mit Askaridenextrakt bei fluchtigen eosinophilen Lungeninfiltraten, Helvet. med. acta. **11**: 117 (April) 1944.
6. Lavier, G.; Bariety, M., and Caroli, J.: Distomatose hépatique et syndrome de Loeffler, Paris méd. **29**: 434 (May 20) 1939.
7. Hoff, Amanda, and Hicks, H. Mason: Transient Pulmonary Infiltrations: A Case with Eosinophilia (Loeffler's Syndrome) Associated with Amebiasis, Am. Rev. Tuberc. **45**: 194 (Feb.) 1942.
8. Gravesen, Poul Bondo: Transitory Lung Infiltrations with Eosinophilia. Acta med. Scandinav. **96**: 523 (nos. 5-6) 1938.

For the present it may be assumed that Loeffler's syndrome is an allergic reaction that can be provoked by a variety of allergens. The relationship of tropical eosinophilia to Loeffler's syndrome is not clear; according to Apley and Grant [9] the two conditions are similar and are not clearly distinguishable.

Current Comment

THE 1945 ANNUAL SESSION IN PHILADELPHIA

As indicated under the Organization Section in this issue of THE JOURNAL, the Board of Trustees, through authority vested in it by the constitution of the Association, has transferred the annual session for 1945 from New York City to Philadelphia. The dates are June 18 to 22 inclusive. Because of the tremendous demands on the hotels for rooms, physicians are asked to cooperate by refraining from making a reservation in more than one hotel, also by limiting their reservations to the minimum amount of space that they need to occupy. Physicians are asked to share accommodations by utilizing a double room with another physician whenever that is convenient. The medical profession of Pennsylvania and of Philadelphia and all of the groups in Philadelphia concerned in the holding of this session promise to do their utmost to aid the success of the meeting.

MATURITY AND THE COMPLETION OF HIGHER EDUCATION

The average age of students who complete their formal programs of higher education, including that in medicine, has shown a consistent rise during the past century. The only exception has been the recent reversal due to the war. Pressey,[1] who has recently reviewed the history of this trend in the United States, points out that many efforts have been made to counter this development over the same period. A great variety of evidence, he says, medical, psychologic, educational and sociologic, indicates that maturity of the human organism is reached at about 20 and that thereafter only a relatively few years remain at prime. Before the war the average age of obtaining the M.D. degree was 28; consequently many of the best years are spent in learning rather than in "doing." Pressey's plea is that completion of programs of higher education is desirable—preferably about two years earlier than was usual before the war. In the field of medical education this problem is peculiarly complex; the subject deserves discussion and study, but decision as to the desirability of a shortened course with graduation at an earlier age should not be unduly influenced by the abnormal conditions of medical training which exist during the war.

9. Apley, John, and Grant, G. H.: Eosinophilia with Pulmonary Disease on Return from the Tropics, Lancet **2**: 303 (Sept. 2) 1944.

1. Pressey, Sidney L.: A Neglected Crucial Psychoeducational Problem, J. Psychol. **18**: 217 (Oct.) 1944.

UNUSUAL BRAVERY OF THE MEDICAL CORPS

The heroic and self-sacrificing acts of many men of the medical corps have been repeatedly noted under Medicine and the War in THE JOURNAL. Feats of combat pilots, gunners, submarine crews, pioneer troops and tank crews are frequently vividly described in the newspapers. Physicians with the armed services are daily performing great and small acts of heroism in the care of the sick and injured. Often their work is unnoticed beyond the small group in which they regularly do their professional duties. A War Department release of November 19 announces the award of the Silver Star to five men, of whom three were members of the Medical Corps of the Army of the United States. Among twenty-two men awarded the Bronze Star Medal, seven were medical officers and eight enlisted men of the Medical Department. Nearly all of the citations were given for the high devotion to duty displayed by medical officers in going to the aid of wounded soldiers in the face of intense enemy infantry and artillery fire with utter disregard for their own personal safety. This record all doctors may share with pride.

THE TRANSFORMATION OF NORMAL CELLS INTO CANCER CELLS

In his review of recent work on cellular transformations, Haddow [1] pays special attention to cytoplasmic mechanisms in cancer. In cell division different characters in cells with the same nuclear genes may result from a differential segregation of cytoplasmic constituents and "determiners." The change of normal cells into cancer cells is a most remarkable transformation. This change occurs spontaneously, and experimentally it can be produced by cancerigenic chemicals, x-rays and other radiations. Generally speaking, the change involves more or less loss of differentiation with gain in the rate of growth. Not infrequently specific differentiation cannot be recognized. The change is permanent and irreversible—the cancer cell continues to multiply as such in the original host, in transplants to new hosts and in cultures outside the body. But this multiplication is not dependent on the presence of the agent which started it. As Haddow puts it "it is patent that the carcinogen does not provide the real stimulus to growth, since growth proceeds without it. Hence the mechanism which permits unlimited growth must clearly reside in the cell itself." What the carcinogen appears to do is to change permanently the normal mode of growth of the cells, and this change is inheritable. In the light of the current developments in cytogenetics it is Haddow's conclusion that the mechanisms of the unlimited growth of the cancer cell "may reside partly at least in the cytoplasm."

1. Haddow, A.: Transformation of Cells and Viruses, Nature **154**: 194 (Aug. 12) 1944.

MEDICINE AND THE WAR

ARMY

CONFERENCE OF FLIGHT AIR SURGEONS

Top flight air surgeons from all fighting theaters recently conferred at the AAF Personnel Distribution Command, Atlantic City, and assumed duties of flight surgeons consultant in army general and service forces regional hospitals all over the country. Specially selected by the chief of the Professional Services Division, they will confer with hospital authorities on aviation medical matters and visit air forces patients and discuss individual problems relative to transfer to AAF medical facilities or to duty on a flying status in the Air Forces through the PDC.

Top flight air surgeons at the conference: Standing, left to right: Major A. A. Sprong, Sterling, Kan., from Hawaii and the South Pacific; Major D. E. James, Belvidere, Ill., China-Burma-India theater; Major L. M. Kistler, Los Angeles, India; Capt. J. H. Arrington Jr., Columbia, Mo., eye, ear, nose and throat specialist; Major G. R. Elliott, Orange, Va., European theater; Capt. E. W. Furgurson, Plymouth, N. C., India, Burma; Major J. M. Smolev, Erie, Pa., Southwest Pacific; Major H. W. Cummings, Greenfield, Mass., Africa; Major B. H. Bennett, Washington, D. C., Australia, New Guinea; Capt. A. J. Gantz, Greenfield, Iowa, Central Pacific. Seated, left to right: Major R. C. Page, Carmel, N. Y., chief, Professional Services, AAF, Washington, D. C.; Major F. L. Spann, Fort Worth, Texas, chief of Professional Standards Branch, Professional Services; Major P. P. Leone, Philadelphia, former registrar, Surgeons Division.

ARMY AWARDS AND COMMENDATIONS

Major Clarence S. Livingood

Major Clarence S. Livingood, formerly of Philadelphia, has been awarded the Bronze Star Medal with a citation from the Commanding General for some as yet unpublished work which cannot be described because of censorship requirements. The citation reads "for meritorious service in connection with military operations against the enemy . . . to provide information which would obviate the extension of this disabling condition in American troops. His work reflected great credit on himself and on the Medical Department." Dr. Livingood graduated from the University of Pennsylvania School of Medicine, Philadelphia, in 1936 and entered the service Feb. 15, 1941.

Captain George R. Conner

Capt. George R. Conner, formerly of Kirksville, Mo., was recently awarded the Soldier's Medal. The citation accompanying the award read "When a plane hit an obstruction and crashed during a take-off on June 14, 1944 in the Far East, he and an ambulance driver proceeded to the scene. The wrecked aircraft was burning rapidly, creating an imminent danger of the high octane gasoline or the bomb load exploding. He climbed along the wing until he ascertained that the pilot was not in the forward cockpit, while the ambulance driver searched the rear section for the gunner. With 0.50 caliber ammunition exploding from the plane they also searched the area until first one crew member and then the other were located from 200 yards away. During this time the bombs exploded while these men were only 40 yards from the wreckage. Escaping injury, they administered to the injured fliers, who were then removed to a hospital. The complete disregard for personal safety displayed by them reflects great credit on themselves and the military service." Dr. Conner graduated from the University of Louisville School of Medicine in 1936 and entered the service Aug. 10, 1942.

Captain Harold C. Rosenthal

Capt. Harold C. Rosenthal, formerly of Poughkeepsie, N. Y., was recently cited by Lieut. Gen. S. B. Buckner Jr., commanding officer of the Advance Command Post, Headquarters Alaska Defense Command. The citation reads "Reports have reached me from several sources concerning the splendid service rendered by you to U. S. Army troops wounded at Attu and being evacuated in your ship. Your untiring effort and professional skill greatly alleviated the suffering of our troops during their trying voyage. I wish to convey my appreciation of your magnificent work and trust we may be so fortunate as to have the benefit of your services again in this theater." Dr. Rosenthal graduated from Cornell University Medical College, New York, in 1929 and entered the service Aug. 13, 1942.

DISTINGUISHED MEDICAL OFFICERS HONORED AT WINTER GENERAL HOSPITAL

The Winter General Hospital, Topeka, Kan., has adopted the plan of naming its important clinics, buildings and streets for distinguished deceased medical officers of the Army who so far have never been honored by having their names given to buildings, general hospitals or other entities of the Medical Department, U. S. Army. The names are selected as appropriate for the particular clinic or building. The names of the streets are those of medical officers who have become the heads of other branches of the Army. The following are the names so far selected:

The Waterhouse Medical Clinic, named for Surgeon Benjamin Waterhouse (1754-1846) of Massachusetts, who introduced vaccination in America and was first professor of medicine at Harvard.

The John Jones Surgical Clinic, named for Surgeon John Jones (1729-1891) of New York, who wrote the first American medical book, founded the New York Hospital and was first professor of surgery at King's College, now Columbia University.

The Northington Roentgenological Clinic, named for Col. Eugene Garland Northington (1880-1933) of Alabama, pioneer student of military roentgenology, who lost both arms and finally his life from cancer due to exposure to the rays before their danger was known to science.

The Rodriguez Dental Clinic, named for Major Fernando Emilio Rodriguez (1888-1932) of Puerto Rico, who made the first studies of the bacteriology of dental caries.

The Keen Neurosurgical Clinic, named for Major Williams Keen (1837-1932) of Pennsylvania, pioneer student—with his colleagues Acting Assistant Surgeons Silas Weir Mitchell and George Reed Morehouse—of gunshot wounds of nerves and one of the few medical officers who served in both the Civil War and the first world war.

The Rush Neuropsychiatric Clinic, named for Surgeon General Benjamin Rush (1745-1813) of Pennsylvania, author of the first American book on insanity, the only systematic American treatise on the subject before 1883, signer of the Declaration of Independence and founder of the University of Pennsylvania.

The Shippen Clinic for Women, named for Director General William Shippen Jr. (1736-1808) of Pennsylvania, first teacher of obstetrics in America, first professor of surgery in America and founder of the University of Pennsylvania.

The Woodward Laboratory, named for Lieut. Col. Joseph Janvier Woodward (1833-1884) of Pennsylvania, pioneer in photomicrography, eminent anthropologist and President of the American Medical Association.

The names of other important clinics, buildings and streets after distinguished deceased officers of the Army were published in THE JOURNAL, July 24, 1943, page 878.

AVIATION MEDICAL EXAMINERS

Graduation exercises for a class of medical officers who have successfully completed the Aviation Medical Examiners' Course were held October 13 at the School of Aviation Medicine, Randolph Field, Texas. The graduation address was made by Brig. Gen. Aubrey Hornsby, chief of staff, AAF Central Flying Training Command, Randolph Field, Texas. Presentation of the diplomas was made by Brig. Gen. Eugen G. Reinartz, school commandant.

MEDICAL ADMINISTRATIVE CORPS OFFICER HONORED

Lieut. Ralph H. Major Jr., M. A. C., formerly of Kansas City, Mo., aide de camp to General Hume in Italy, has been awarded the Cross of War for Military Valor by the Italian government. The presentation was made by Gen. Roberto Beneivenga, who was Italian military commander of Rome at the time of the Allied entry last June. The citation declared that Lieutenant Major has "shown great devotion to duty under shell fire in connection with the capture and administration of the city of Rome." Last June Lieutenant Major was presented with the Magistral Cross of the Sovereign Military Order of Malta by Prince Ludovico Chigi Albani, grand master of the famous order of knighthood, which was founded in the twelfth century.

WOMEN'S ARMY CORPS PERSONNEL MAY BE ASSIGNED TO SANITARY CORPS

According to a recent release from the Sixth Service Command, Chicago, provisions of section X, Circular No. 333, War Department, 1944, as far as they pertain to bacteriologists, biochemists and serologists, apply to enlisted women of the Women's Army Corps. Such personnel may be appointed second lieutenants in the Women's Army Corps for assignment and immediate detail in the Sanitary Corps. Officers appointed under this authority who later prove unsatisfactory are subject to the provisions of AR 605-230. They may be reassigned within the Medical Department. Under no condition will officers so appointed be reassigned outside the Medical Department.

PROMOTION AND NEW ASSIGNMENT FOR COLONEL PADEN

Lieut. Col. Paul A. Paden, Cleveland, former director, Military Personnel Division, has been promoted to colonel and assigned as chief of the Personnel Service, Office of the Surgeon General, relieving Col. J. R. Hudnall, who has been assigned as executive officer of Walter Reed General Hospital, Washington, D. C. Colonel Paden has been in the Office of the Surgeon General since 1941, where he was first executive officer in the Military Personnel Division, becoming director in 1943. He graduated from the University of Tennessee College of Medicine, Memphis, in 1932 and entered the service in 1934. Prior to coming to the Office of the Surgeon General, Colonel Paden was executive officer of the Station Hospital at Fort Riley, Kansas.

COLONEL ASH APPOINTED DIRECTOR OF ARMY INSTITUTE OF PATHOLOGY

Col. James E. Ash has been appointed director of the Army Institute of Pathology, Army Medical Museum. His title was formerly that of curator. He recently made an extended trip through the North African and other theaters of war in the interests of the Museum and Medical Arts Services. The museum is undertaking to supply all medical schools in the United States and Canada with material for research and training in tropical diseases. Lieut. Col. Balduin Lucke, who was acting curator during the absence of Colonel Ash, has been named deputy director.

ARMY DENTAL CORPS CONFERENCE

Dental surgeons representing the twelve major Army Air Force commands met in conference recently at the headquarters of the Second Army Air Force, Colorado Springs. The conference, planned and guided by Col. George R. Kennebeck, D. C., Chief of the Dental Branch, Professional Service Division of the Air Surgeon's Office, and his assistant, Lieut. Col. Raymond C. Turk, D. C., marks the first such event for Army Air Forces command dental surgeons.

MENTAL HYGIENE COMMITTEE HONORS GENERAL KIRK

The National Committee for Mental Hygiene has elected Major Gen. Norman T. Kirk, Surgeon General of the Army, as one of its six new members, in recognition of his "unusual awareness of the importance of skilled psychiatric treatment in the Army.

HEADS SIXTH SERVICE COMMAND

Brig. Gen. Russel B. Reynolds was recently appointed to succeed Major Gen. R. S. Aurand as commanding general, Sixth Service Command. General Aurand's new assignment has not as yet been made public.

NAVY

PHYSICAL TRAINING ROUTINE ORDERED IN NAVAL HOSPITALS

Vice Admiral Ross T. McIntire, Surgeon General of the Navy, set in operation recently a system of organized physical training for patients in all continental naval hospitals and convalescent hospitals. The program, established under the Rehabilitation Branch, Professional Division, Bureau of Medicine and Surgery, calls for "physical exercise of graded intensity" for patients to minimize "the deterioration in physical fitness which accompanies confinement to bed" and thus reduce the number of sick days. Physical training thus becomes part of the daily naval hospital routine and of the general treatment plan. Exercise for individual patients will, however, be confined to activities which the responsible medical officer deems appropriate and will not exceed limitations set by him.

To facilitate assignment of patients to appropriate physical training, patients will be classified in the following groups: (1) Ambulant—no limitations on physical activity, (2) Ambulant but with stated restrictions on physical activity, (3) Confined to ward, (4) Confined to bed, (5) No activity. This phase of the Navy's rehabilitation program will be carried on under the command of medical officers by physical training officers graduated from the school established recently at the Naval Training Center, Sampson, N. Y. The first group completed the course on October 21 and subsequent groups will follow at weekly intervals. Personnel selected for this work by the Bureau of Naval Personnel majored in physical education in civil life and in many instances had experience in corrective exercises. Their indoctrination includes many of the features of a "refresher course" in physical education. To insure further uniformity in their activities, each physical training officer is furnished a manual of carefully selected, graded physical activities satisfactory to the Bureau of Medicine and Surgery which may be followed without interruption when a patient is transferred from one hospital to another.

Complements of physical training personnel who come under the cognizance of the Bureau of Naval Personnel but who are under the command of medical officers in command will be assigned to hospitals on an approximate basis of one officer to 1,000 patients and one specialist (A) to each 100 patients.

NAVY NEEDS 3,000 DOCTORS

Vice Admiral McIntire, who is chief of the Bureau of Medicine and Surgery, stated recently that 3,000 more physicians will be required by the Navy because personnel expansion and intensification of naval operations in the Pacific area has precipitated a grave shortage of medical officers. Admiral McIntire told Mr. Paul V. McNutt, chairman of the War Manpower Commission, that "with less than 13,000 medical officers on active duty in the Navy the procurement of at least 3,000 more as soon as possible is imperative."

The Army will fill its future requirements for military physicians from sources now available and therefore will not require future certification of availability of additional physicians from the Procurement and Assignment Service of the War Manpower Commission.

THE NAVY'S REHABILITATION PROGRAM

Vice Admiral Ross T. McIntire, surgeon general of the Navy, recently stated that "proper rehabilitation starts the day a man is wounded or breaks down." The Navy, therefore, has developed a broad program which involves a number of new ideas and is showing bright promise. "No man is so handicapped," the surgeon general said, "that he cannot become a useful citizen. So far as it is in the Navy's power, no disabled man will be returned to his community without being well equipped physically and psychologically. Whatever has happened, the disabled man is taught that he still has a valuable place to fill in the world. The chaplains, who play a valued part in rehabilitation, do much to replace despair and bitterness with hope and a healthy, optimistic outlook."

In this counterattack on disability, encouraging victories are being won. There are very few men who have been blinded. In the Philadelphia Naval Hospital, where the blind ultimately are brought for training, there are not more than a score of these patients, including men blinded by the sort of mishaps common in civilian life. They are trained to live a full and normal life, trained to take up civilian status with assurance. Highly encouraging work also is being done with the deaf. Excellent procedures have been worked out in the treatment of amputations and the training of amputees. If a man has lost an arm or a leg, a plastic substitute exactly suited to his needs is made in the hospital by skilled craftsmen working in constant collaboration with the surgeons. It is routine that these men learn to drive an automobile and to dance. A great many are permitted to return to military duty. Others go into civilian life at trades learned while they are recuperating.

OFFICIAL NAVAL MEDICAL HISTORY OF THE WAR

Capt. Louis H. Roddis (MC), U.S.N., twice editor of the *Naval Medical Bulletin*, reported for duty at the Bureau of Medicine and Surgery October 30 and has been made responsible for the preparation of the official naval medical history of the war. He recently completed thirty-one years of naval service.

NAVY AWARDS AND COMMENDATIONS

Lieutenant John E. Stewart

The Legion of Merit medal was recently awarded to Lieut. John E. Stewart, formerly of Juneau, Alaska. The citation reads "For exceptionally meritorious conduct in the performance of outstanding services to the government of the United States as a medical officer during action against enemy Japanese forces on Tarawa atoll, Gilbert Islands, Nov. 20, 1943. Although hampered by heavy enemy antiboat gun, machine gun and sniper fire, at extreme risk of his own life, he made his way to the wounded men and administered aid to them and displayed marked ingenuity in utilizing rubber boats to convoy the wounded men through the surf. On November 22 he volunteered to take six corpsmen to an area of heavy fighting, and under heavy enemy machine gun fire he maintained an aid station under extremely difficult and dangerous conditions. Through his resourcefulness in the use of an amphibian tractor for the evacuation of wounded, and through his courage, endurance and devotion to duty, many lives were saved that might otherwise have been lost. His conduct throughout was in keeping with the highest traditions of the naval services." Dr. Stewart graduated from Harvard Medical School, Boston, in 1941 and entered the service in September 1942.

Lieutenant Commander Tracy D. Cuttle

Lieut. Comdr. Tracy D. Cuttle, formerly of Philadelphia, has been awarded the Bronze Star Medal "for meritorious service while serving as senior medical officer of a tank landing ship operating in the Solomon Islands area from August 1943 to April 1944. Lieutenant Commander Cuttle, by his highly intelligent planning, professional ability, initiative and untiring efforts was largely responsible for equipping and training his own and other tank landing ships so that the medical service of these vessels was greatly improved, which undoubtedly resulted in the saving of many lives. The improvements were performed under adverse circumstances when equipment was difficult to obtain and numerous improvisations were necessary. His accomplishments were of inestimable value and his conduct and devotion to duty throughout were in keeping with the highest traditions of the United States Naval Service." Dr. Cuttle graduated from the University of Pennsylvania School of Medicine, Philadelphia, in 1935. He entered the service in 1940.

Captain George B. Dowling

The Distinguished Service Medal was recently awarded to Capt. George B. Dowling, formerly of Washington, D. C. His citation reads "For exceptionally meritorious service to the government in a duty of great responsibility, as staff medical

officer of a task force of United States Naval Forces in Europe, during the period Nov. 29, 1943 to July 20, 1944. Captain Dowling, by his part in the planning for an operation of the system of evacuation of the wounded from the continent to the United Kingdom by LSTs, has made a significant contribution to the war effort. His experience, ability, wisdom and energy were invaluable in the solution of the many intricate problems involved. The personal and enthusiastic assistance rendered by Captain Dowling in every undertaking of this important task resulted in the ameliorating of much suffering and in the saving of many lives." Dr. Dowling graduated from George Washington University Medical School, Washington, D. C., in 1917 and was appointed to the Navy in the same year.

Commander Jasper L. Custer

The Bronze Star Medal was recently awarded to Comdr. Jasper L. Custer, formerly of Shreveport, La. The citation accompanying the award read "For meritorious performance of duty as Senior Medical Officer of the U. S. S. *Block Island* when that vessel was . . . sunk by enemy action on May 29, 1944. Commander J. L. Custer unhesitatingly went to the aid of a man pinned between the wreckage of the port forward catwalk and the ship's side and gave what medical aid and comfort was possible while attempts were being made to free him. After it became evident that it would be necessary to amputate the man's leg if he was to be freed before the ship sank, Commander Custer performed the operation under extremely hazardous and unfavorable conditions and succeeded in releasing the man in time to remove him from the rapidly sinking ship. Commander J. L. Custer's calm and efficient performance of duty in the face of great danger was an inspiration to the entire crew and was in keeping with the highest tradition of the United States Naval Service." Dr. Custer graduated from the University of Texas Medical Branch, Galveston, in 1927 and entered the service April 6, 1942.

Lieutenant Mark W. Wolcott

The Air Medal was recently awarded to Lieut. Mark W. Wolcott, formerly of Philadelphia, for "meritorious achievement in aerial flight as crew member of an R4D transport plane attached to the South Pacific Air Transport Command from July 15 to 25, 1943. When his craft was unable to land on the densely overgrown jungle terrain while transporting urgently needed supplies to our forces on New Georgia Island, Lieutenant Wolcott skilfully performed his duties and rendered invaluable assistance to his pilot in accurately dropping the cargo as the unarmed plane flew in at terrific speed and at tree top level to avoid intense enemy antiaircraft fire and aerial opposition, making several hazardous runs on the targets to complete the mission and frequently returning to base without the protection of covering planes. Lieutenant Wolcott's cool courage and unwavering devotion to duty under extremely difficult conditions contributed materially to the success of these vital missions and were in keeping with the highest traditions of the U. S. Naval Service." Dr. Wolcott graduated from the University of Pennsylvania School of Medicine, Philadelphia, in 1941 and entered the service July 15, 1942.

MISCELLANEOUS

WARTIME GRADUATE MEDICAL MEETINGS

The following subjects and speakers for Wartime Graduate Medical Meetings have just been announced:

U. S. Naval Hospital, San Diego, Calif.: Surgery of the Chest, Dr. Leo Eloesser, November 30.

U. S. Naval Hospital, Philadelphia: Recent Physiologic and Pharmacologic Studies Bearing on Respiration, Dr. Carl Schmidt, December 1; The Common Cold, Influenza, Dr. Hobart A. Reimann, December 15.

Crile General Hospital, Cleveland: Bone Grafting, Dr. James A. Dickson, December 12.

Camp McCoy, Wisconsin: Endocrinology, Dr. Elmer L. Sevringhaus, November 29; Virus and Rickettsial Diseases, Dr. Marcos Fernan-Nunez, December 13.

U. S. Naval Hospital, Great Lakes, Ill.: Diagnosis and Treatment of Acute Suppurative Meningitis, Dr. Paul S. Rhoads, December 5; The Physiology of Respiration as It Affects Thoracic Surgery, Dr. Ralph B. Bettman, December 19.

THE NETHERLANDS FACING FAMINE AND EPIDEMICS

The Netherlands Information Bureau reports that the Dutch people are now faced with a dangerously rising death rate caused by the shortage of food and fuel. One of the most alarming symptoms of the people's lowered resistance is the increase in tuberculosis, a direct cause of which is malnutrition. At the beginning of this month the diet for the inhabitants of the larger cities dropped to less than 900 calories a day. By international standards a person who sits quietly all day engaging in no activities whatever requires a minimum of 1,200 calories each day, while any one who does a normal day's work needs from 2,500 to 4,000 calories. Margarine and butter supplies were completely exhausted by November 1; in Amsterdam and Haarlem there is no flour for the baking of bread, while in other cities all flour will be gone soon.

Unless the cities of the Netherlands are liberated within a short time, the disaster will assume gigantic proportions. Owing to the complete lack of fuel, the pumping stations, which supply the Dutch people with their drinking water, will soon cease to operate. Holland's intricate sewerage system will also come to a standstill and an outbreak of epidemics of the worst sort may be expected.

PLACEMENT PROGRAM FOR VETERANS

Northrop Aircraft, Inc., Hawthorne, Calif., recently developed a placement program by which veterans of this war, particularly those with physical handicaps, may be intelligently moved into industry. The Northrop placement program begins at Birmingham General Hospital at Van Nuys, Calif., where the company has established an airplane production department. It contains machines, tools and all equipment necessary for light metal shop work. Convalescents, nearly all of whom are overseas casualties, are given a short training course and then start on actual production, for which they are paid standard shop rates. When these men are discharged for return to civilian life they are encouraged to take employment at the main Northrop plant. On recovery the veteran who is discharged is adjusted to a special type of work and readily fits into this work. This is primarily for the physically handicapped or injured. Dr. Harold B. Dye, chief surgeon at Northrop Aircraft, Inc., stated that the same basic plan could be worked out for the mentally handicapped. Agencies should be established in connection with hospitals to assure a round peg being placed in a round hole. The United States Employment Service is of assistance in finding work for veterans but is not able to approach the subject from the standpoint of specialized work for the physically and mentally handicapped.

RED CROSS SENDS PENICILLIN BY AIR FOR PRISONERS OF WAR IN GERMANY

The American Red Cross has sent 5,000 tubes of penicillin by air express to the International Red Cross Committee in Geneva to be used for American prisoners of war held by Germany. The Red Cross plans additional shipments of medicines and medical supplies for prisoners of war. The International Committee has been asked to keep the prison camp leaders informed of the medicines available in the stocks held in Geneva for their use and to suggest that the leaders not allow camp stocks to become depleted before reordering.

Regular shipments of Red Cross first aid kits intended for use when doctors are not available have been made to the prison camps in Germany. Bulk shipments of medicine and medical supplies also have been made to supplement those provided by German military authorities for the care of sick and wounded prisoners of war.

ORGANIZATION SECTION

Official Notes

THE 1945 ANNUAL SESSION

The Ninety-Fifth Annual Session of the American Medical Association will be held in Philadelphia June 18 to 22, 1945. This session was originally scheduled to be held in New York June 11 to 15, but because of untoward conditions growing out of the war emergency it was found that needed facilities would not be available in that city.

A very cordial invitation has been extended to the Association by the Philadelphia County Medical Society to hold the 1945 session in that city. The Philadelphia Convention and Tourists Bureau, the Hotel Association, those concerned with the operation of transportation facilities and other civic groups have given assurances that everything possible will be done to contribute to the success of a meeting in Philadelphia. Final arrangements are being made as rapidly as possible.

Hotel Reservations

Hotel reservations will be made through a central office in Philadelphia. It is highly desirable that reservations be made as early as possible. Those who expect to attend the Philadelphia session are urgently requested to refrain from making reservations in more than one hotel. In numerous instances at the annual session held in Chicago in 1944, and at other sessions previously held, individual physicians have made reservations at two or three hotels and on arrival at the place of meeting have completed their reservations at one hotel and failed to cancel other reservations. The result has been that many physicians have found it impossible to secure accommodations. If this practice is persisted in it will become increasingly difficult for the Association to find a satisfactory place of meeting.

At the Chicago session several hotels had a large number of reservations which they had made in good faith only to find that multiple reservations made by individuals, which were not needed, were not canceled, and the result was that the hotels had vacant accommodations, which after a short time were given over to persons who were not concerned with the annual session of the American Medical Association.

Washington Letter

(From a Special Correspondent)

Nov. 20, 1944.

Medical Stand on Extension of Social Security Considered

A determined move is under way in Congress for extension of social security. It is expected that extension of social security will ultimately be achieved and, when this happens, social security taxes must go up. Another argument, not connected with the extension issue, is now raging on the question of doubling social security taxes next year on both employers and employees. More than 50 million people are affected. The administration favors the doubling, but House and Senate leaders close to the subject are against it, as in several previous years. The "pro" argument is that the terms of the Social Security law should be carried out now because so many people are making money. The "against" argument is that so much money has already been earmarked for future social security payments, on the basis of benefits under the present law, that it would be unnecessary and unwise to increase the tax burden.

Senator Arthur Vandenberg, Republican, of Michigan, made his fourth annual move to freeze the rate at the present 1 per cent level. He argues that at existing pay roll rates the social security reserve (now estimated at more than 6 billion dollars in government bonds) is from eight to twelve times the contemplated annual drain on the fund in the next five years.

House and Senate tax committee leaders have tentatively moved to compromise the 1 per cent tax increase, now scheduled to take effect automatically January 2. Instead of the 2 per cent doubled rate on workers and employers starting New Year's day, they propose to spread the increase over two years. Under the plan, still in renegotiation, the tax would be moved up to 1.5 per cent in January 1945 and would not reach the full 2 per cent rate until January 1946.

President Asks Year's Compulsory Training for Young Persons

President Roosevelt told his latest White House press conference that he hopes Congress acts this winter on legislation requiring the youth of the nation to give a year's service to the government. Seemingly aware of opposition of both Protestant and Catholic church leaders, the President did not commit himself on whether compulsory training should be military. The President recalled physical benefits gained by youths who went through the Civilian Conservation Corps program. He pointed out that the CCC boys did not have military training but benefited greatly from their experience. He said that a universal training program would give the nation a large number of young people trained to defend the country in the event of future wars. The Army favors compulsory training to make it possible to mobilize four million men overnight, and several bills along this line have been introduced in Congress.

Service Chiefs Ask for Increased Blood Donations

An appeal for increased blood donations was made here by Vice Admiral Ross T. McIntire, Surgeon General of the Navy, and Major Gen. Norman T. Kirk, Surgeon General of the Army. Increasing casualties in both Europe and the South Pacific are necessitating air shipments of whole blood to both battle fronts. The service chiefs have pointed out that among those who have given blood are a number of men in service who themselves have faced death and suffered wounds. Many World War I veterans, they added, have been consistent blood donors. Whole blood is shipped daily from Washington and New York to Europe, and regular shipments go from the West Coast to the South Pacific. A new method had to be devised to keep blood fresh on its long journey via Naval Air Transport Service from San Francisco to Pearl Harbor and then to island bases.

Army Medical Research Board to Continue in Peace

Brig. Gen. James S. Simmons, chief of the preventive medicine service in the Office of the Surgeon General, U. S. Army, told the meeting of the National Academy of Sciences here that plans are being made for an Army Medical Research Board to continue in peacetime to seek ways to protect army health for better defense of the nation. Correlated with the proposed Army Medical Research Board, under present plans, would be a committee on Medical Research for developing within civilian institutions medical investigations of importance to the armed forces. The Army board would include one member of the civilian committee, which in turn would have one member from the Army board, to provide closest cooperation.

Society Proceedings

COMING MEETINGS

American Society of Anesthetists, New York, Dec. 14. Dr. McKinnie L. Phelps, 745 Fifth Ave., New York 22, Secretary.

Association for Research in Nervous and Mental Diseases, New York, Dec. 15-16. Dr. Thomas E. Bamford Jr., 115 E. 82d St., New York 28, Secretary.

Puerto Rico, Medical Association of, Santurce, Dec. 15-17. Dr. E. Martinez-Rivera, P. O. Box 3866, Santurce, Secretary.

Southern Surgical Association, Hot Springs, Va., Dec. 5-7. Dr. Alfred Blalock, Johns Hopkins Hospital, Baltimore 5, Secretary.

Western Surgical Association, Chicago, Dec. 1-2. Dr. Arthur R. Metz, 250 East Superior St., Chicago, Secretary.

WINNEBAGO COUNTY MEDICAL SOCIETY PLAN

Edwin G. Quattlebaum Jr., M.D.
ROCKFORD, ILL.

In early 1942 most members of the Winnebago County Medical Society were aware of increasing interest in medical social security. Some of the membership realized how difficult it was for the average busy physician to keep in close touch with the needs, desires and demands of the people. A committee was established to be known as a Public Relations and Planning Committee. Its major functions were:

1. To keep itself posted on trends of public thought and on ways and means of meeting requests of the public for increased medical service.
2. To keep the membership of the society advised as to these trends and their extent.
3. Possibly to some extent to mold public opinion.

The committee's membership was almost unanimously opposed to governmental administration of medical services under the Surgeon General of the U. S. Public Health Service or under any other individual. The committee was convinced that medical service to the American public could be increased through prepaid medical care programs in which the individual could obtain partial reimbursement by paying the premium directly out of his pocket rather than through taxation.

It soon became obvious that several fundamental principles should be kept in mind. First, the absolute right of any patient to select his own physician without any restraint, interference or pressure from any source, and the right to do this at any time, should be maintained. Second, the patient-physician relationship should be carefully guarded. Third, the premium should be low so as to reach the average family. It was our desire that the plan should not prepay all expenses. We wanted something similar to the automobile collision deductible policy, which meets the bulk of auto accident costs without encouraging careless driving and unwarranted claims. Moreover, we believed that a total payment plan would have a tendency to influence fees. Fourth, it was felt that under no circumstances should the fee be paid directly to a physician, so as to avoid any semblance of self interest or collusion between insurance carriers and physicians. The ideas were in keeping with those developed in the House of Delegates of the American Medical Association.

As time went by it became apparent that no plan yet devised met, in every respect, the principles listed. Throughout the country plans were beginning to be developed, most of which were based on the idea of a group of physicians caring for a group of patients for an annual fee. This, to our way of thinking, interfered with the unlimited choice of physicians on the part of the patient and for that reason did not meet with our approval. Further, most of the plans developed in the beginning did not attempt to care for medical as well as surgical disabilities, and we felt that this should be attempted.

Fortunately for our community, a Blue Cross plan for partial prepayment of hospital care had been organized under the able direction of Mr. F. F. Armstrong, executive secretary, and, with the cooperation of the physicians and hospitals of the community, had done an outstanding job. The success of the nonprofit hospital plan in Winnebago County led us in the beginning to consider an extension of Blue Cross, to include reimbursement of medical expenses, but we learned that the hospital service could not enter the medical-surgical field until the Illinois state legislature passed an enabling act.

The county medical society authorized the committee to aid in passage of an enabling act. This procedure, of course, requires time and there are dangers. The greatest danger is that unless the act is painstakingly worded it might be possible for unethical organizations to practice medicine. In any event the Illinois legislature was not to meet until January 1945.

Rather than to await passage of such an act, we began to consider commercial plans and soon discovered that we were unable to find any that attempted to meet the overall ideas we had in mind. Fortunately, about this time we learned that one of the larger writers of accident and health insurance in this country was considering the idea of trying such a plan in a small way. As a result of this discovery our conversations with the North American Accident Insurance Company began. This organization was interested, and after considerable discussion between members of the committee and executives of this company a tentative plan was worked out. At this time the committee took to the county medical society a request for the adoption of two resolutions:

1. That the society go on record as approving the development of any prepaid medical care plan which would meet the prerequisites listed.
2. That the committee be empowered to approve the plan submitted by the North American Accident Insurance Company.

The two resolutions were adopted.

The plan submitted by the North American Accident Insurance Company is experimental, to be tried in Winnebago County only until such time as an actuarial experience can be developed which might warrant its wider use.

This particular commercial insurance company has been most cooperative. It has agreed, for example, that official advertising done would be released only after its approval by the planning committee of the Winnebago County Medical Society. It has also agreed that, if the experience in this community warrants, the plan will be rapidly liberalized. At present, unfortunately, if the plan is to be sold at low cost it is necessary that it contain some exclusions and exceptions.

The Winnebago County Medical Society has no desire to sponsor any one insurance carrier. On the contrary, it hopes that every reputable insurance carrier in the United States will see fit to sponsor and sell such plans, not only elsewhere in the country, but also in this community. Just as we feel that the free choice of a physician on the part of a patient makes for better medical care, we feel that competition among insurance carriers, profit and nonprofit, is most advantageous to the public. This community, therefore, is anxious to support any plan that meets the specifications outlined and feels that, the more organizations that can be developed, the more rapidly low cost prepaid medical care plans may be obtained by the public.

Briefly, the plan approved by this committee as presented by North American Accident Insurance Company is as follows:

The plan will partly reimburse the patient for medical expenses thus:

A fee of $2 per call in the event of any disabling illness on the part of husband or wife up to 65 years of age and any dependent member of the family between the ages of 3 months and 18 years. The fee is to be paid regardless of whether the call is made in a physician's office, in a hospital or in the patient's home. The first two calls are deducted, being left to the patient to pay. In the event that the disability is due to accident, payment begins for first call. The total paid by the insurance carrier in any one illness for any one member of the family shall not exceed $250 in any one year. The total for all children shall not exceed $500 in any one year. The total for husband and wife shall not exceed $500 in any one year. In the event of a surgical disability, in lieu of the $2 per call the patient may elect to take a flat surgical fee, which fee favorably compares with fees provided in standard accident and health policies.

The premium charge for the foregoing shall be $3 per month, less 10 per cent for an annual premium paid in advance. This provides for the entire family of husband, wife and any dependent children between the ages of 3 months and 18 years. Single persons obtain protection at proportionately lower cost.

There are other exceptions and exclusions, most of which are minor, and it is sincerely hoped that the plan will be sufficiently successful from an actuarial point of view to warrant the rapid elimination of many of these minor exclusions.

It would not be fair to close this article without expressing for the committee its great appreciation of the help, courtesies and kindnesses extended to us by the American Medical Association, particularly its legal department, the National Physician's Committee for the Extension of Medical Care and representatives of local newspapers.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Changes in Health Personnel.—Dr. Harrison Eilers, health officer of San Luis Obispo, has been appointed health officer of Long Beach, succeeding Dr. Frank W. Stewart, who resigned November 1. Dr. Andrew M. Harvey, assistant health officer, has been named acting health officer until Dr. Eilers takes over his new work about January 1.

Personal.—Morris A. Stewart, Ph.D., associate professor of parasitology, College of Agriculture, University of California, Berkeley, has returned to the university after three months spent in South America (THE JOURNAL, July 22, p. 858), chiefly in Bolivia, as consulting parasitologist to the government. While there he was made honorary professor of parasitology of the Instituto Superior de Medicina Veterinaria and the Instituto Orientale de Biologia.

Human Death from Rabies.—A 3 year old child died in September in Albany following the bite of a rabid dog, according to *California's Health*, official bulletin of the state department of health. The dog strayed into Albany, where it was killed by a policeman after it had bitten the child. One dog bitten by the animal and 2 contacts are still under observation. The bulletin emphasizes the need for preventive measures and for the exercise of rigid control over dogs and cats in those communities where rabies is known to be present. During the past year the disease has been found in Kern, Imperial, Tulare, Kings, Fresno, Los Angeles, Monterey, Napa, Contra Costa, Riverside, Sacramento, San Bernardino, San Diego, San Luis Obispo, Santa Cruz, Solano, Sonoma, Stanislaus and Alameda counties. The latest area to be included is the east shore of San Francisco Bay, particularly in Berkeley, Albany, El Cerrito, Richmond and Crockett. The examination by the state laboratory of the head of a dog which had bitten a man and a woman in Berkeley proved the presence of the disease in the animal.

CONNECTICUT

Society Creates Section on Surgery.—Dr. Paul W. Vestal, New Haven, has been appointed chairman and Drs. Donald B. Wells, Hartford, chairman-elect, and Andrew J. Jackson, Waterbury, secretary-treasurer of the newly created section on surgery of the Connecticut State Medical Society.

Building Fund.—At a meeting of the council of the Connecticut State Medical Society, October 10, the trustees of the society's building fund were directed to proceed at once with a fund raising program to obtain contributions for $50,000 to provide a building for the society's headquarters. The first meeting to discuss preliminary plans was held October 25.

Statewide Peacetime Blood Bank.—The council of the Connecticut State Medical Society has appointed a special committee to confer with a similar committee from the Connecticut Hospital Association to discuss a proposed plan to continue, if possible, the community blood and plasma banks that have been developed during the war. Members of the committee are Drs. Ralph E. Kendall, Hartford, chairman; John C. Leonard, Hartford, Karl T. Phillips, Putnam, Arthur J. Geiger, New Haven, and Irving B. Akerson, Bridgeport.

DELAWARE

State Journal Has New Address.—The *Delaware State Medical Journal* announces that its new address is 822 North American Building, Wilmington 7. For two and one-half years the *Journal* was located at 618 Citizens Bank Building, but the new owners of the building, the North American Mutual Insurance Company, have renamed it the North American Building. The state journal now occupies larger quarters in the renamed building.

DISTRICT OF COLUMBIA

Personal.—Major Alfred Golden, M. C., who has been on duty for the past four years at the Army Medical Museum, has been transferred to the division of health and sanitation, Office of the Coordinator of Inter-American Affairs.

Child's Death from Rabies Called "Unique."—On November 1 a positive rabies report was issued by Dr. John M. Byers, health officer of Prince Georges County, Md., in the death of a 16 year old boy of Mount Rainier, Md., October 19. Newspapers stated that the case would be one of the most unusual in medical history if the parents' assumption is true that the boy was infected with rabies some fourteen months ago by his pet dog. The dog was taken to a hospital on Labor Day 1943 after he acted "peculiar" and appeared to be sick. Several days later, it was stated, the dog died after he had apparently strangled himself in a net at the hospital. No examination for rabies was performed. It was pointed out by the attending physician that no bite would have been necessary from the pet dog, as the boy could have become infected through saliva through scratches on the skin. The physician said the boy showed no signs of any illness all the time he supposedly carried the deadly infection. He became ill suddenly October 13, was taken to George Washington University Hospital October 15 and died there four days later. In March a 65 year old woman died at Gallinger Municipal Hospital, five months after being bitten by a rabid dog, and in November 1943 a soldier stationed in Washington died after being infected by a dog.

ILLINOIS

Changes in Health Personnel.—Ruth Sumner, Ph.D., has been appointed acting chief of the division of public health instruction, Illinois State Department of Public Health, during the leave of absence of Leona de Maré East, A.B., who is continuing her graduate training in health education at the University of North Carolina School of Public Health.——Dr. Donaldson F. Rawlings, Cairo, has resigned as health officer of the Alexander-Pulaski County Health Unit to enter the U. S. Navy.——Dr. Samuel S. Reinglass, Dixon, resigned as health officer of Lee County, effective October 1, to enter private practice in Canton, Ohio.

Chicago

Personal.—Dr. Howard Glenn Gardiner, Chicago, has resigned as medical director of Foote Brothers Gear and Machine Corporation, effective November 20, to become associate medical director of Oldsmobile division of General Motors, Lansing, Mich.

Dr. Ivy to Address Institute of Medicine.—Dr. Andrew C. Ivy, Nathan Smith Davis professor of physiology and pharmacology, Northwestern University Medical School, will deliver the presidential address at the twenty-ninth annual meeting of the Institute of Medicine of Chicago, December 5, at the Palmer House, on "Contributions to Survival on a Raft at Sea."

KANSAS

Personal.—Dr. Vernon M. Winkle, director of the district health unit at Gering, Neb., has been named epidemiologist and assistant director of the health department of the Topeka-Shawnee Health Department; he will also be in charge of the school health services of the unit.

Graduate Medical Clinic.—The fall clinic on obstetrics and pediatrics, sponsored by the Kansas Medical Society, the state board of health and the University of Kansas School of Medicine, was held at the Lassen Hotel, Kansas City, November 2-3. The principal speakers were Drs. Julian D. Boyd, associate professor of pediatrics, State University of Iowa College of Medicine, Iowa City, and M. Edward Davis, professor of obstetrics and gynecology, University of Chicago School of Medicine.

Jayhawker, M.D.—The October graduating class of the University of Kansas School of Medicine, Lawrence-Kansas City brought out the first student annual for publication by the medical class of the school. The volume is a testimonial to the members of the faculty, to the many students in all classes and to the school itself. It is replete with photographs of teachers, students and school buildings. The book is a splendid tribute to the efforts of the recent graduating class. In its own defense, editorially, the class rejects the comment passed at some time during its career that it was the worst class the school had seen in thirty-one years.

Free X-Rays at State Fair.—A feature of the Kansas Free Fair in Topeka this year was the offer of chest x-rays to all who cared to have them. Of 5,000 visitors at the exhibit during the week of the fair, 1,129 were given roentgenograms which disclosed 18 cases of significant tuberculosis hitherto unreported to the state board of health. Two were in persons in the age group 15-24, 8 in the age group 25-44, 3 in the age group 45-64, and 5 persons more than 65 years

of age. In addition to these eighteen patients, all of whom were referred to their family physicians, 15 persons were advised to consult their physicians because of lesions suggestive of tuberculosis and 15 others showed chest or heart conditions which warranted further examination by a physician. The public health building at the fair, which has been under the supervision of the state board of health since 1936, was devoted entirely this year to tuberculosis education. The Topeka Tuberculosis Association and the division of tuberculosis control of the state board of health cooperated.

MARYLAND

Dr. Williams Reappointed.—Dr. Huntington Williams has been reappointed commissioner of health of Baltimore for a six year term. He has held the position since January 1933, after having first served as director of health from Oct. 1, 1931.

Society News.—The Baltimore City Medical Society was addressed November 17 by Dr. Edward M. Hanrahan, Baltimore, on "Indications for and Procedures Used in Breast Plastic Operations" and Col. Thomas Fitz-Hugh, M. C., "A Medical Officer's Experiences in a Jungle Theater of Operations."

University News.—The department of pharmacology of the University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, has received a gift of $4,000 from the Ohio Chemical and Manufacturing Company of Cleveland to establish a fellowship for the study of volatile anesthetics, especially "propethylene," under the direction of John C. Krantz Jr., Ph.D., professor of pharmacology.

MASSACHUSETTS

Licenses Revoked.—At a meeting of the Massachusetts Board of Registration in Medicine, September 13, the license to practice medicine of Dr. Mary E. Bolger, Worcester, was revoked because of violation of her probationary period as of Feb. 10, 1942 and the license of Dr. Don D. Cornell, Pilcher, Okla., formerly of Boston, because of the violation of the Harrison Narcotic Act.

John Downing Named Professor at Tufts.—Dr. John G. Downing has been appointed professor of dermatology and syphilology at Tufts College Medical School, Boston, and chief of the department of dermatology and syphilology at Boston City Hospital, the *Harvard Medical Alumni Bulletin* for October announced. Dr. Downing is also professor of dermatology at Boston University School of Medicine and dermatologist in chief at the Massachusetts Memorial Hospitals.

MONTANA

Osteopaths Defeated in Montana.—On November 7 the Montana voters defeated an Initiative, Number 48, a bill that would have given Montana osteopaths "unlimited surgical rights" and would have defined osteopathy as a branch of medicine with its own ruling board. The bill was defeated almost two to one. Credit in the defeat of the bill is ascribed to the Public Health League of Montana, a recently formed group with offices in Helena including dentists of the state, the Montana Hospital Association, the Catholic Hospital Association, Montana State Medical Association, Montana State Nurses Association, Optometric Association, Hospital Service Association of Montana, Montana Tuberculosis Association, state division of the Field Army, pharmacists of the state and many other interested groups. Mr. Joseph L. Markham, Butte, newspaperman, was designated campaign manager against the bill, and the Montana State Medical Association was represented by its officers and a special seven man committee.

NEBRASKA

Ninety-Two Years of Age.—Dr. John A. Waggener, Humboldt, observed his ninety-second birthday in October. According to the *Nebraska State Medical Journal*, Dr. Waggener observed the day attending to his practice as usual.

NEVADA

State Medical Election.—Dr. Moreton J. Thorpe, Reno, secretary of the Nevada State Medical Association, writes that at the recent meeting of the state medical association Dr. Daniel J. Hurley, Eureka, was reelected president. Dr. Hurley had been elected in 1942 to take office as president, but soon afterward he was called into service leaving his term unfilled. Dr. Lemuel R. Brigman, Reno, was at the same time president-elect, so he automatically assumed the office in Dr. Hurley's place in 1942 and then in his own right became president in 1943, causing his presidency to run two years, through the unfilled term of Dr. Hurley and his own. These circumstances left Dr. John R. McDaniel Jr., Las Vegas, as president-elect. He was to take office in 1942 as president, but when he was called into service the association chose Dr. Hurley. Dr. Thorpe points out that two president-elects were called into service at almost the same time. Dr. Hurley is now president and Dr. McDaniel president-elect.

NEW YORK

Memorial to Physician.—A campaign is under way in Pavilion to collect funds to create a Dr. Sweeting Memorial Fund in honor of the late Dr. Sherman C. Sweeting, who practiced in the community for more than fifty years. The memorial will honor the physician and be used as Pavilion's contribution to the campaign under way to build in Batavia a new Genesee Memorial Hospital.

New Consultant Named for Silicosis.—Dr. Edward G. Whipple, Rochester, has been appointed a special consultant to the state department of labor on dust diseases, notably silicosis, to succeed the late Dr. John J. Lloyd, Rochester. Dr. Whipple will serve with Drs. Edgar Mayer and J. Burns Amberson Jr., New York, on the commission, which was established by the state legislature some years ago. Dr. Whipple will have charge of the Buffalo-Rochester districts.

Paul Lembcke to Direct Temporary Commission of Medical Care.—Dr. Paul A. Lembcke, Rochester, district number 4 health officer, under leave of absence granted by the New York State Department of Health, has been appointed director of study for the New York State Temporary Commission of Medical Care, according to the Rochester *Democrat and Chronicle*. Dr. Lembcke served as state epidemiologist in 1939. Offices of the commission have been opened in the Terminal Building, Rochester.

Teaching Day on Rheumatic Fever.—November 30 has been designated teaching day on rheumatic fever and rheumatic heart disease at Syracuse University College of Medicine. Among the speakers will be:

Dr. T. Duckett Jones, Boston, Etiology, Epidemiology and Diagnosis of Rheumatic Fever and Rheumatic Heart Disease.
Dr. Albert D. Kaiser, Rochester, Treatment of Rheumatic Fever.
Dr. Homer F. Swift, New York, Prevention of Recurrences in the Known Rheumatic Patient.
Dr. David D. Rutstein, Albany, Need for a Public Health Program for the Care of the Rheumatic Child.

A dinner meeting will be addressed by Dr. Brewster C. Doust, professor of pediatrics at Syracuse. Among the agencies sponsoring the day's program will be Cayuga, Cortland, Onondaga and Oswego county medical societies, the state medical society, the state department of health and the university.

New York City

License Restored.—The license to practice medicine of Dr. Millicent Morden, Brooklyn, which had been suspended for one year, was reinstated by the state education department on September 22.

Max Bergmann Dies.—Max Bergmann, Ph.D., a member of the Rockefeller Institute for Medical Research and prominent for his work in organic chemistry, died at Mount Sinai Hospital, November 7, aged 58.

Medical Bequest.—Under the will of the late Henry R. Ickelheimer, a private banker, Cornell University will receive $25,000 for cancer research, according to *Science*. There is also a provision for $42,500 for Mount Sinai Hospital.

Personal.—Dr. Andrew J. Warren, who has been associated with the International Health Division of the Rockefeller Foundation since 1921, has been appointed assistant director.——Dr. William H. Kahrs was recently guest of honor in celebration of his completion of fifty years in the practice of medicine.

The Janeway Lectures.—Dr. Otto Loewi, research professor of pharmacology, New York University College of Medicine, gave the Edward Gamaliel Janeway lectures at Mount Sinai Hospital, November 13, on "Aspects of the Transmission of the Nervous Impulse" and one November 15 on "Theoretical and Clinical Implications."

OHIO

Personal.—Milton J. Foter, Ph.D., has recently been appointed head of the department of bacteriologic research of the William S. Merrell Company, Cincinnati.——Dr. James Howard Holmes, Toledo, has been appointed a member of the Ohio Public Health Council to fill the unexpired term of the late Dr. Ward D. Coffman, Zanesville, which will end June 30, 1950. ——Dr. Johnson S. Hunter, Jackson, recently completed fifty years in the practice of medicine.

Physicians Honored.—A portrait of the late Dr. Asa Brainerd Isham, who died in 1912, one of the founders of the Cincinnati General Hospital and a former president of the Cincinnati Academy of Medicine, was recently presented to the hospital by the children of Dr. Isham.——Drs. Charles I. Thomas and William E. Bruner received the distinguished service award of the Cleveland Community Fund for outstanding work in the field of sight restoration.

Fifty Thousand Dollars for Study on Proteins.—Swift & Company, Chicago, has given a special grant of $50,000 to the University of Cincinnati for a five year research project on proteins and their role in rehabilitating persons disabled by nutritional deficiencies. The study is to be carried on at the Hillman Hospital, Birmingham, Ala., under the direction of Dr. Tom D. Spies, associate professor of medicine, University of Cincinnati College of Medicine. Since 1936 Dr. Spies has been directing work in this field both at the university and at the Hillman Hospital, where he is director of the Nutrition Clinic.

PENNSYLVANIA

Lester Perry Appointed Executive Secretary of State Society.—Mr. Lester H. Perry, A.B., since 1934 manager of sessions and exhibits of the Medical Society of the State of Pennsylvania, has been appointed executive secretary. Mr. Perry, who joined the state medical society after serving as executive secretary of the Allegheny County Medical Society, graduated at the University of Pittsburgh in 1925.

Annual Postgraduate Day.—The Harrisburg Academy of Medicine held its annual postgraduate day in Harrisburg, November 16. The program constituted a seminar by the following members of the faculty of Ohio State University College of Medicine, Columbus:

Laurence H. Snyder, Sc.D., Importance of the Hereditary Background in Medical Diagnosis, Prognosis, Prevention and Treatment and Current Medical Significance of the Blood Groups, with Special Reference to the Rh Factor.

Dr. George M. Curtis, Diseases of the Parathyroid Glands and Their Management and Surgical Considerations in Splenic Disease.

Dr. Charles A. Doan, Differential Diagnosis and Treatment of the Anemic States and Increasing Significance of the Pathologic Physiology of the Spleen in Clinical Medicine.

Philadelphia

Hospital News.—The name of the National Stomach Hospital has been changed to the Physicians and Surgeons Hospital, effective October 15.

Personal.—Dr. William B. Griggs, who has completed fifty years in the practice of medicine, was guest of honor at a dinner November 1 given by members of the staffs of St. Luke's and Children's Medical Center and the Women's Homeopathic Hospital.

The Pancoast Memorial Lecture.—The fourth Henry K. Pancoast Memorial Lecture was presented before the Philadelphia Roentgen Ray Society and the College of Physicians of Philadelphia, November 2, by Dr. Edward B. Benedict, Boston. Dr. Benedict's subject was "The Correlation of Gastroscopic, Roentgenologic and Pathologic Findings in Lesions Involving the Stomach."

SOUTH DAKOTA

Personal.—Dr. Clarence E. Sherwood, Madison, has been appointed to the state board of health to fill the unexpired term of the late Dr. James B. Vaughn, according to the *Journal Lancet*.——Dr. Frank W. Haas, assistant superintendent of the Yankton State Hospital at Yankton, has been appointed by the governor to the commission for control of feebleminded, succeeding the late Dr. George S. Adams.

TEXAS

Dr. Painter Named Acting President of University of Texas.—Theophilus S. Painter, Sc.D., research professor of zoology, University of Texas, Austin, has been made acting president of the university.

Changes in Hospital Superintendents.—Included among the recent changes in hospital superintendents of the state hospitals are the following: Dr. Roy Cameron Sloan, assistant superintendent, Terrell State Hospital, Terrell, superintendent, to succeed Dr. William Thomas, who retired September 15; Dr. Bruce Allison, assistant superintendent, Wichita Falls State Hospital, Wichita Falls, to succeed Dr. Monroe A. Beckman at the Abilene State Hospital, Abilene, effective September 1, and Dr. David McCullough, assistant superintendent of the State Tuberculosis Sanatorium, Sanatorium, superintendent of the Kerrville State Sanatorium, Kerrville. Dr. McCullough succeeds Dr. Henry Y. Swayze, who resigned September 1 to enter private practice.

VIRGINIA

Personal.—Thomas Gordon Bennett, Ph.D., formerly of the U. S. Public Health Service and once superintendent of schools for Calvert and Queen Anne's counties, Md., has been appointed consultant in health education to the Virginia Department of Education.

State Medical Election.—Dr. Julian L. Rawls, Norfolk, was named president-elect of the Medical Society of Virginia at its meeting in October and Dr. Henry B. Mulholland, Charlottesville, was inducted into the presidency. Miss Agnes V. Edwards, 1200 East Clay Street, Richmond 19, is the secretary. The 1945 session will be held in Roanoke.

Changes in Health Personnel.—Dr. Glenn H. Baird has resigned as venereal disease control officer of the Richmond City Health Department to become health officer of the Smyth-Washington-Bristol Health District, with headquarters in Abingdon.——Dr. William B. Bailey, Montgomery, W. Va., has been appointed health director for Norfolk and Princess Anne counties.——Dr. Donald K. Freedman, U. S. Public Health Service, has been named health officer of district number 5, Williamsburg, to succeed Dr. William W. Fuller, who resigned to enter the armed forces, effective November 1.

WASHINGTON

Hospital News.—On October 15 the cornerstone of the new Doctors Hospital, Seattle, was laid at special ceremonies of the board of trustees of the King County Medical Service Corporation (THE JOURNAL, Dec. 18, 1943, p. 1059).

Personal.—Dr. Herbert A. Perry, assistant superintendent of the Eastern State Hospital, Medical Lake, has been appointed superintendent. He succeeds Dr. Marinus W. Conway, who will enter private practice after serving in the position for eleven years.——Dr. John H. O'Shea, Spokane, was guest of honor at a banquet at the Davenport Hotel, August 10, in recognition of his completion of thirty-five years with the Spokane fire department.——Dr. Edward B. Riley, Aberdeen, has been appointed temporary coroner of Grays Harbor County to succeed Dr. Joseph H. Fitz, Montesano, resigned.

WEST VIRGINIA

State Association Acts to Remove Politics from Health Program.—At a meeting November 9 the council of the West Virginia State Medical Association unanimously adopted a legislative program providing for:

The appointment by the governor of a state health commissioner from a list of three names or more to be submitted by the council of the West Virginia State Medical Association.

The appointment of medical members of the Public Health Council from a panel of three names for each position to be filled, to be submitted to the governor by the council of the West Virginia State Medical Association.

The appointment of superintendents of state eleemosynary institutions from a list of names to be submitted to the governor by the Public Health Council.

The council recommended that the Barboursville unit of the Weston State Hospital be reestablished as a unit of the Huntington State Hospital, that $100,000 be appropriated for each year of the biennium for cancer control and that the arrangement with the Medical College of Virginia, Richmond, for the admittance of twenty students annually from the two year medical school at West Virginia University, Morgantown, be continued. Both committees and the council devoted a good deal of time to the consideration of an enabling act in connection with the operation of hospital-medical-surgical plans in this state. The present act passed at the 1943 session of the legislature becomes inoperative Feb. 28, 1945. Solution of the problem was left to the legislative committee, which was instructed to consult with similar committees from the hospitals and hospital-medical service groups in drafting a bill to be introduced in the legislature in January. The association has already approved a basic contract for use by component societies in connection with the establishment of medical-surgical service plans over the state. The council also approved in principle the extension of Farm Security Administration service plans to provide medical and hospital service to certain families in the low income group in every part of the state. Sixteen such plans have already been established. The council recommended the establishment of a department of public health at West Virginia University and approved the university's plan to ask for an appropriation for a new building for the two year school of medicine. Approval was also given to the following items in the state health department's legislative program: antepartum serologic examination for syphilis, transfer of the crippled children's division from the department of public assistance to the state health department, transfer of the supervision of the superintendents of the state eleemosynary institutions from the board

of control to the public health council, creation of a dental hygiene division, increase in the salary of the state health commissioner and construction of a separate building on state property near the capitol to house all divisions of the state health department.

GENERAL

Examinations in Otolaryngology.—The American Board of Otolaryngology will conduct examinations at the Waldorf-Astoria, New York, June 5-8, and at the Palmer House, Chicago, October 3-6.

National Public Health Nursing Day.—The first National Public Health Nursing Day will be held throughout the country on January 26. The theme of the observance will be "Know Your Public Health Nurse—Who She Is, What She Does." In charge of details is the National Organization for Public Health Nursing, Inc., 1790 Broadway, New York 19.

1945 Public Health Meeting.—The executive board of the American Public Health Association announces that the third wartime conference and seventy-fourth annual meeting, and meetings of related organizations, will be held in Chicago, September 17-23, with headquarters in the Hotel Stevens. The related organizations will include the American School Health Association and the Conferences of State and Municipal Public Health Engineers, of Public Health Nursing Directors, of Professors of Preventive Medicine, of State and Provincial Public Health Laboratory Directors, of State Directors of Public Health Education and of Industrial Health Consultants. The Illinois committee in charge of local arrangements will be headed by Dr. Herman N. Bundesen, president, Chicago Board of Health, and Dr. Roland R. Cross, state director of public health, Springfield, co-chairmen. The headquarters office of the American Public Health Association is located at 1790 Broadway, New York 19. Dr. Reginald M. Atwater is executive secretary.

Southern Surgical Association.—The fifty-sixth annual session of the Southern Surgical Association will be held at the Homestead, Hot Springs, Va., December 5-7, under the presidency of Dr. Alton Ochsner, New Orleans. Among the speakers will be:

Dr. William F. Rienhoff Jr., Baltimore, Analysis of the Results of the Surgical Treatment of Peptic Ulcer of the Duodenum in a Series of 260 Cases.
Lieut. Col. James Barrett Brown and Capt. Bradford Cannon, M. C., Repair of Gunshot Wounds of the Face and Jaws.
Dr. Louis T. Byars, St. Louis, Color Matching of Skin Grafts and Flaps by Pigment Injection.
Lieut. Col. Alfred R. Shands Jr. and Major Randolph L. Clark Jr., M. C., Surgical Problems in Aviation Medicine.
Lieut. Col. Brian B. Blades, M. C., Penicillin as an Adjunct to the Surgical Treatment of Acute and Chronic Empyemas.
Drs. Loyal Davis, George E. Perret and Walter W. Carroll, Chicago, Surgical Principles Underlying the Use of Grafts in the Repair of Peripheral Nerve Injuries.
Drs. Thomas B. Aycock and Edward M. Farris, Baltimore, Effects of Sulfonamides on the Mortality Rate in Acute Appendicitis.
Drs. Roy D. McClure and Conrad R. Lam, Detroit, End Results in the Treatment of Hyperparathyroidism.
Lieut. Col. Lloyd G. Lewis, M. C., Cases of Severe Injury to the Pelvis.
Drs. Kenneth L. Pickrell, Durham, N. C., and Richard K. Richards, Chicago, Pentothal-Metrazol Antagonism: A Method of Shortening the Recovery Period Following Pentothal Anesthesia; A Clinical and Experimental Study.
Drs. Warfield M. Firor and George O. Gey, Baltimore, Observations on the Conversion of Normal into Maliganant Cells.
Dr. John M. T. Finney Jr., Baltimore, and Lieut. Murray L. Johnson (MC), Primary Carcinoma of the Gallbladder.
Dr. Everett I. Evans, Richmond, Va., Studies on Traumatic Shock: V. The Treatment of Clinical Shock with Gelatin.
Drs. Gameel B. Hodge, Keith S. Grimson and Herman M. Schiebel, Durham, Surgical Results of a Revival of Radical One Stage Excision and Stripping of Varicose Veins Coupled with Pressure Bandages and Early Activity.

Public Health Cancer Association Formed.—The Public Health Cancer Association was recently organized to meet the particular need of persons engaged in cancer control activities in federal, state, city and other official agencies. Active membership is limited to professional workers in such official cancer programs, and officers include Drs. Herbert L. Lombard, Boston, president; Raymond V. Brokaw, Champaign, Ill., vice president, and Morton L. Levin, Albany, N. Y., secretary-treasurer. Included in the membership of the executive committee are Drs. Frank L. Rector, Lansing, Mich., Louis C. Kress, Albany, and Edmund G. Zimmerer, Des Moines, Iowa. Representatives attending the organization meeting felt that the American Association for Cancer Research adequately covered that field, that the American Cancer Society is chiefly engaged in lay educational work and that the new organization would meet the particular needs of full time employees engaged in cancer work in the official agencies. It was also felt that such an association would be of value in furthering cancer control by conducting an annual meeting and a cancer symposium in connection with the annual session of the American Public Health Association. While representatives from about eleven states attended the organization meeting, the membership will not be limited solely to this group.

LATIN AMERICA

Health Activities in Latin America.—*Physicians Studying in the United States.*—Among Latin American physicians who are studying in the United States are Drs. Germano Brasiliense Bretz, Brazil, who will go to the Johns Hopkins University, Baltimore; Guillermo Grebe H., tuberculosis specialist connected with the Chilean National Medical Service for Employees, who will do research work in his specialty at Columbia University College of Physicians and Surgeons, New York; Elias Motles, connected with the Sanatorio El Peral of Santiago, Chile, who will study at the Trudeau Sanatorium, Saranac Lake, N. Y.; Jose Decusati, Brazil, who will pursue studies in urology at the Massachusetts General Hospital, Boston; Adhemar Paoliello, connected with the Brazilian public health service of Rio de Janeiro, who will study at Johns Hopkins University, Baltimore, and Albino Figuereido, specialist in antepartum hygiene, who will study maternal and child hygiene at the University of Michigan Medical School, Ann Arbor. All of these persons, with the exception of Dr. Paoliello, will first complete a short course in English before continuing with their studies in their specialties.

Mexico's Health.—More Mexican patients die from diarrhea and enteritis than from any other disease, it was revealed by the latest mortality figures released by the Mexican Ministry of National Economy. The government statistics, which embrace the years from 1938 to 1942, show that these conditions take an average toll of 90,504 lives annually and that their mortality rate is 45.66 per 10,000. Occupying second place in the ministry's study is pneumonia, which is responsible for an average of 67,560 deaths a year, or a mortality of 34.12 per 10,000. The number of yearly deaths due to other illnesses, and their corresponding mortality rates, are, in the order of their importance, malaria, with an average of 25,454 deaths a year and a mortality rate of 12.9 per 10,000; congenital diseases and those of early childhood, 18,289 and 9.74 per 10,000; whooping cough, 12,893 or 6.5; bronchitis, 12,386 or 6.24, and tuberculosis, 11,066 or 5.6.

Surgical Meeting.—The sixth assembly of Mexican surgeons was held at the Juarez Hospital, Mexico City, November 19-25. Speakers and the fields in which they gave papers include Traumatology, Drs. Pablo Mendizabal, Jose Castro Villagrana, Alfonso Ortiz Tirado, Alejandro Castanedo, and Alejandro Malo; Urology, Drs. Eduardo Castro, Adalberto Parra, Aquilino Villanueva, Manuel Pesqueira, Alberto Madrid, Herbert Stacpoole, and Carlos Aguirre; Neurosurgery, Drs. Clemente Robles, Mariano Vasquez, Alfonso Aceves Zubieta F., Manuel Sanchez Garibay and Miguel Lavalle; Throat and Thorax, Drs. Donato G. Alarcon, Carlos Jimenez Caballero and Julian Gonzalez Mendez; Gynecology, Drs. Conrado Zuckermann, Rosendo Amor, Arturo de los Rios, Genaro Zenteno, Fernando Perera Castillo, Gilberto Sousa and Abelardo Monjes Lopez; Obstetrics, Drs. Manuel Mateos Fournier, Jose Rabago, Isidro Espinosa y de los Reyes and David Fragoso; Pediatrics, Drs. Jesus Lozoya, Guillermo Christy and Vicente Roqueni; Gastroenterology, Drs. Abraham Ayala Gonzalez, Jose Aguilar Alvarez, Gustavo Baz, Jose Gaxiola Gandara and Raul Pena Trevino; General Military and Emergency Surgery, Col. Gustavo Gomez Azcarete, Major Rafael Moreno Valle and Drs. Rafael Vargas Otero, Jose Rojo de la Vega, and Alfonso Diaz Infante. There also were sections devoted to ophthalmology and dental surgery.

CORRECTIONS

Dr. Henrik Dam.—In the editorial in THE JOURNAL, November 4, page 640, concerning the Nobel Prize Awards, it was stated that Dr. Henrik Dam is assistant professor of biochemistry at the University of Rochester School of Medicine and Dentistry, Rochester, N. Y. Dr. Dam is senior research associate at the university, not assistant professor.

Brazilian War Bread.—The first four lines of the Brazil letter in THE JOURNAL, July 22, page 863, should read "Dr. Castro Barretto, Head Advising Physician of the Technical Department of Nacional Feeding, Ex-Regular Professor of Clinical Medicine of the Faculty of Medicine of Rio de Janeiro and member of the Institute of Brazilian Studies, recently presented a report with the results of his studies on war bread to the Coordinator of Economic Mobilization. The report was approved by the War Bread Commission which was appointed by the Coordinator to study it. The author stresses . . ."

Foreign Letters

LONDON

(From Our Regular Correspondent)

Oct. 22, 1944.

Improved Vital Statistics Continue: Highest Birth Rate for Nineteen Years

In previous letters the astonishing fact has been reported that our vital statistics have actually improved. The Ministry of Health has just announced the registrar general's returns for the June quarter of 1944 showing that the higher wartime level of the birth rate in England and Wales, for which an explanation has been suggested in previous letters, was more than maintained. A birth rate of 19.3 per thousand of population is recorded. This is the highest rate of any second quarter since 1925 and compares with a rate of 17.5 in the corresponding period last year and 17.9 for the first three months of this year. There were 199,326 births registered. Of these 102,603 were boys, giving a proportion of 1,061 boys to 1,000 girls. The average proportion of boys to girls for the ten preceding second quarters was 1,056 to 1,000.

For the second quarter in succession a new low record for infant deaths was established. A provisional rate of 43 per thousand related live births was 11 below the average of the ten preceding second quarters and was the lowest rate for any June quarter. The general death rate was 11.2 per thousand, compared to 14.2 in the preceding three months and 10.9 for the second quarter of last year. For the same period from 1938 to 1942 the average rate was 12 per thousand. The births exceeded the deaths by 83,801. Corresponding excesses in the second quarters of 1942 and 1943 were 50,674 and 67,802 respectively. Marriages numbered 82,215 and exceeded by 95 those for the corresponding quarter last year. But they were 23,460 fewer than the average for the same period of the years 1938-1942. This falling off is explained by the fact that allowances introduced at the outbreak of war have left comparatively few young people of marriageable age and circumstances unmarried today.

British Prisoners Killed in Allied Air Raids on Germany

In answer to a question in the House of Commons, Mr. Law, minister of state, said that it was unfortunately true that a number of British prisoners of war have lost their lives in allied air raids on the continent, but as the figures could not be given with any accuracy he would not attempt an estimate of them. Under the German prisoner of war system there are main camps to which are attached subsidiary work camps and detachments forming several thousand units scattered all over the country. Some of these camps have been or are situated near legitimate military targets, contrary to article 9 of the Geneva Convention. All available information as to the location of the camps is promptly passed to the Allied air forces and is used in briefing air crews. Whenever the delegates of the protecting power during their periodic visits to camps have observed that our prisoners were dangerously close to a military target they have immediately complained to the German authorities and demanded the transfer of the camp to a safer site. Also the British government made strong representations to the German government through the protecting power. But, Mr. Law regretted to say, in several instances the German authorities have not complied with these demands. As an additional precaution the German authorities have been urged to provide adequate air raid protection for our prisoners. There was no evidence to show that casualties in prisoner of war camps said to be due to bombing were in fact executions, he added.

Neglect of Clinical Examination for Laboratory Tests

From time to time feminine teachers issue a warning against the neglect of thorough clinical examination in favor of a multitude of laboratory tests. Thus J. A. Ryle has said that in the past quarter of a century the main endeavor of medicine has been to discover new diagnostic methods. Countless improvements have been due to roentgenology, chemistry and endoscopy, but symptomatology has suffered neglect. Professor Ryle pleaded for a wider and closer clinical study of disease. The current number of the *Army Medical Department Bulletin* presents an article entitled "Clinicians and Special Departments," which points out that in the medicine of today the final and conclusive piece of diagnostic evidence is often supplied by the pathologist or radiologist. But this is bad if it leads physicians to lose their clinical sense, instincts and judgment by turning first to special departments.

The case is quoted from the *Lancet* of a pallid, wasted, elderly man who had suffered from intestinal symptoms for nearly six months. He had a large bundle of documents, which included twelve reports on elaborate examinations of his feces and eight on his blood. There was much about the Arneth count, as it shifted more or less to the left on occasion. At times the hemoglobin rose 1 or 2 per cent from an average of 65 per cent, an improvement regarded as worthy of congratulation. The sedimentation rate was carefully scrutinized. Though invariably accelerated, it exhibited minor variations regarded as of great consequence. The work on the urine comprised every possible sort of investigation. The diagnosis was an atypical infection by an anaerobic streptococcus for which intestinal antiseptics had proved disappointingly inadequate. No examination of the abdomen had been made for at least three months, yet a large tumor was palpable there and exploration exposed a huge cyst of the sigmoid.

Civil Defense Casualties

The German bombing of our cities and towns necessitated the formation of civil defense services to deal with the casualties and damage. At the time of the blitz the members employed amounted to 1,500,000; recently the total was 1,200,000. Members of this service have suffered casualties themselves. Addressing a civil defense parade at Birmingham the home secretary, Mr. Herbert Morrison, stated that some 2,000 members had been killed by the enemy, and 8,300 had been seriously injured. There figures did not include casualties to the police and fire services, he added.

Marriages

THOMAS SAMPSON ROYSTER, Henderson, N. C., to Miss Caroline Merck Henry of West Orange, N. J., in Philadelphia, September 23.

LESLIE MORGAN MORRIS, Rutherfordton, N. C., to Miss Mary Alice King of Winston-Salem, September 9.

CHARLES WALTER METZ JR., Denver, to Miss Gloria Evelyn Smith of Nashville, Tenn., September 12.

WILLIAM GORDON LEARY JR., Charlottesville, Va., to Miss Margaret Conley of Cincinnati recently.

RODGER ELLISON MACQUIGG, New York, to Miss Elizabeth Schill of Newark, N. J., September 30.

CHARLES BENJAMIN HANNA, Enoree, S. C., to Miss Lena Mae Bryant of Nichols, September 19.

JOHN DAWSON HARTIGAN, St. Joseph, Mo., to Miss Catherine Leone Fitzpatrick of Omaha recently.

CLARENCE D. LEIPHART, Hellam, Pa., to Miss S. Isabelle Manifold of Bridgeton, October 15.

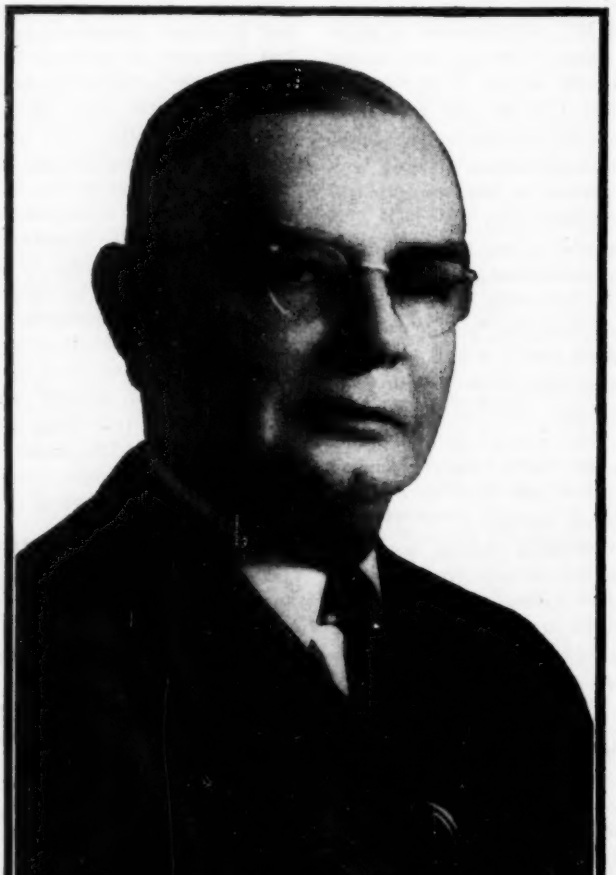
ROY TURNAGE PARKER, Pinetops, N. C., to Miss Georgia Sugg of Hookerton, September 26.

ABRAHAM MELAMED to Miss Hope Goodman, both of Milwaukee, September 3.

Deaths

Edward Marshall Pallette ✠ a member of the Board of Trustees of the American Medical Association since 1942, died suddenly in Chicago November 15 while in attendance on a session of the Board, apparently of an attack of coronary thrombosis. Dr. Pallette was born in Wichita, Kan., Jan. 13, 1874. He received the Ph.B. degree from Northwestern University in 1894 and the Ph.M. in 1895. During 1894 he did investigation in the field of biology as the Oliver Marcy Scholar of Northwestern University at the Marine Biological Laboratory, Woods Hole, Mass. He received the degree of doctor of medicine from the College of Medicine of the University of Southern California in 1898 and then did graduate study in the New York Polyclinic in 1901 and in London, Vienna and Berlin at various times thereafter. He was assistant instructor of zoology at Northwestern University in 1894 and 1895, instructor in biology in the Los Angeles High School from 1896 to 1898 and at the same time instructor in histology and embryology in the College of Medicine of the University of Southern California. Following his graduation in medicine he began medical practice in Los Angeles, giving special attention to gynecology. He was associated with the health department of Los Angeles as assistant health officer from 1898 to 1899 and as a member of the Los Angeles County Board of Health from 1905 to 1906. He taught physiology in the College of Dentistry of the University of Southern California from 1900 to 1912 and was a lecturer in obstetrics and gynecology in the Training School for Nurses of St. Vincent's Hospital.

As a distinguished citizen of the state of California he held many special appointments, including examiner for the California State Lunacy Commission from 1905 to 1915, membership on the California State Board of Public Health from 1932 to 1940 and member of the Retirement Board of the Los Angeles City Schools from 1938 to 1939. Since 1938 he had served also as treasurer and member of the Board of Directors of the Blue Cross Plan known as the Hospital Service of Southern California.



Edward Marshall Pallette, 1874-1944

During World I Dr. Pallette served as a captain in the medical corps, serving as surgeon in the Letterman General Hospital at the Presidio in San Francisco and also at Camp Crane in Allentown, Pa. In the present war he acted as chairman of the Procurement and Assignment Service for Physicians of the War Manpower Commission in southern California. His interest in general education was exemplified by his membership on the Medical School Advisory Committee of the University of Southern California and the presidency of the Los Angeles County Board of Education.

In the work of the American Medical Association, Dr. Pallette gave also fully of himself for the advancement of the medical profession. He was a member of the House of Delegates in 1933, 1935, 1936 and for the period 1938-1942. He was a member of the California State Medical Association and its president in 1936-1937. He was also a former president of the Los Angeles County Medical Association. His membership in special societies included fellowship in the American College of Surgeons, membership in the Los Angeles Surgical Society, the Los Angeles Obstetrical and Gynecological Society, the Los Angeles Academy of Medicine, the Hollywood Academy of Medicine, the Institute of American Genealogy and the American Association for the Advancement of Science. Of many of these groups he had been president.

In the death of Dr. Pallette the American Medical Association lost a loyal and distinguished counselor, a self-sacrificing and devoted member of its Board of Trustees.

Alexis Carrel ✠ Paris, France, died November 5, aged 71. He graduated at the Université de Lyon Faculté de Médecine et de Pharmacie, France, in 1900. He served as prosector at his alma mater until 1902, then came to the United States in 1905 and was appointed to the staff of the Rockefeller Institute for Medical Research in New York in 1906. He was made a fellow in 1909 and a member in 1912 and retired in 1939 as member emeritus. In 1912 Dr. Carrel was awarded the Nobel Prize in Medicine for success in suturing blood vessels and transplanting organs; this was the first time the prize in medicine had been awarded in the United States. He won the Dr. Sofie Nordhoff-Jung Cancer Prize in 1931 and received the eighth Cardinal Newman Award of the Newman Foundation in 1937. In 1937 he received also the Phi Beta Kappa from Dartmouth College. He was presented with the gold service medal award by the New York Rotary Club in 1939.

During World War I Dr. Carrel served as a major in the medical corps of the French army and helped to develop the Carrel-Dakin antiseptic solution for the sterilizing of deep wounds. In 1935, with Colonel Lindbergh, he announced the development of a mechanical heart, in which the heart, kidney or glands from an animal could be kept alive for study in glass chambers supplied by circulation of artificial blood. In 1936 he was appointed Hitchcock professor at the University of California in Berkeley for the spring semester.

Dr. Carrel was an Associate Fellow of the American Medical Association and a member of the American Society for Experimental Pathology, American Surgical Association, the Society of Clinical Surgery, American Society of Physiology, American Philosophical Society, Accademico Pontifico, and the Pontifica Accademia delle Scienze, an honorary fellow of the Royal Society of Medicine, foreign associate Societa Italiana delle Scienze and a corresponding member of various foreign academies. Among other honors he had been decorated Commandeur of the Legion d'honneur, commander of the Order of Leopold of Belgium, member of the Order of the Northern Star of Sweden and commendador de Isabel la catolicà; he received the Distinguished Service Medal and was made a companion of the Order of St. Michael and St. George. He had been a member of the board of the Dazian Foundation for Medical Research, New York, since 1937 and was a trustee of the Institute for Advanced Study from 1930 to 1942.

When war broke out Dr. Carrel joined a special mission for the French Ministry of Public Health, 1939-1940.

He had received the honorary doctor of science degree from Columbia University, Princeton University, University of the State of New York and Manhattan College, the M.D. from Belfast and LL.D. from the University of California. At the time of his death he was director of the Vichy government's Carrel Foundation for the Study of Human Problems. His writing included "Man, the Unknown" and he was joint author with Georges Dehelly of "Treatment of Infected Wounds" and with Charles A. Lindbergh of "The Culture of Organs."

Gardner Weld Allen, Boston; Harvard Medical School, Boston, 1882; member of the Massachusetts Medical Society, American Association of Genito-Urinary Surgeons, Massachusetts Historical Society, American Antiquarian Society, Naval History Society, American Historical Association, Naval Historical Foundation, Essex Institute, Military Historical Society of Massachusetts and the Lincoln Group of Boston; at one time instructor, assistant professor and professor of genitourinary surgery at the Tufts College Medical School; veteran of the Spanish-American War; surgeon, Massachusetts Naval Militia, from 1893 to 1901; formerly surgeon in the genitourinary department of the Boston Dispensary; author of "Our Navy and the Barbary Corsairs," "Our Naval War with France," "A Naval History of the American Revolution," "Massachusetts Privateers of the Revolution" and "Our Navy and the West Indian Pirates"; editor of "Papers of Isaac Hull, Commodore, U. S. Navy," and "Papers of John Davis Long, Secretary of the Navy"; contributor of a chapter of Massachusetts in the War of 1812 to "Commonwealth History of Massachusetts" and eleven naval biographies to the "Dictionary of American Biography"; died July 12, aged 88.

Hugo Erichsen, Birmingham, Mich.; University of Vermont College of Medicine, Burlington, 1882; Detroit Medical College, 1882; Royal College of Physicians and Surgeons, Kingston, Ont., Canada, 1883; professor of neurology at the Quincy College of Medicine, Quincy, Ill., from 1883 to 1885; once city physician of Detroit; past president of the Cremation Association of America; honorary member of the Wayne County Medical Society; member of the Michigan Historical Society and the Michigan Academy of Science, Arts and Letters; for many years affiliated with Parke, Davis & Company and the Burroughs Adding Machine Company in Detroit; in 1932 received the honorary degree of doctor of letters from the College of the City of Detroit; decorated by the French government as Chevalier Ordre du Merite Agricole and Officier d'Académie; assistant editor, *Detroit Clinic,* 1883; associate editor, *Western Medical Reporter,* 1883-1884; editor of the photographic department, *American Boy,* from 1903 to 1913; author of "Medical Rhymes," "Cremation of the Dead," "Methods of Authors" and "Roses and Ashes"; died in the Harper Hospital, Detroit, October 10, aged 84.

Frank Hilton McLeod ✠ Florence, S. C.; University of Tennessee College of Medicine, Memphis, 1888; member of the Southeastern Surgical Congress; past president of the South Carolina Medical Association, Florence County Medical Society and the Tri-State Medical Society; councilor of the Southern Medical Association from 1929 to 1935; fellow of the American College of Surgeons; in 1906 established the Florence Infirmary, now known as the McLeod Infirmary, of which he had been medical superintendent and surgeon in chief; for many years regent at the South Carolina State Hospital, Columbia; awarded the distinguished service plaque for 1941 by the South Carolina department of the American Legion; in 1943 a bronze bust of him was presented to the McLeod Infirmary to mark his many years' service to the community; in 1928 received the Sullivan Award of the University of South Carolina; in 1935 received the honorary doctor of laws from the University of South Carolina; at one time editor of the *Journal of the South Carolina Medical Association;* died October 24, aged 76.

Jerome Joseph McCaffrey ✠ Providence, R. I.; Harvard Medical School, Boston, 1915; member of the New England Society of Psychiatry; a charter member and past president of the Rhode Island Society for Neurology and Psychiatry; served in France during World War I; a first lieutenant in the medical corps of the U. S. Army and adjutant and personnel officer of Evacuation Hospital number 34, American Expeditionary Forces; formerly chief of the State Division of Hospitals and Infirmaries; since 1930 on the neuropsychiatric staff of the Charles V. Chapin Hospital; consultant neurologist at the State Infirmary, Howard; on the neurologic staffs of St. Joseph's Hospital and the Rhode Island Hospital, where he died October 16, aged 56.

Ward Denver Coffman ✠ Zanesville, Ohio; University of Cincinnati College of Medicine, 1919; fellow of the American College of Surgeons; past president of the Muskingum County Academy of Medicine; appointed a member in 1939 and in 1943 chairman of the Ohio Public Health Council; president of the board of education of Zanesville for a second term; served in the medical corps of the U. S. Army during World War I; formerly chief of the staffs of the Bethesda and Good Samaritan hospitals; at one time public school physician at Springfield; died in the Lake-of-the-Woods, Nestor Falls, Ont., Canada, September 7, aged 53, of myocarditis.

Douglas C. Moriarta ✠ Saratoga Springs, N. Y.; Albany Medical College, Albany, 1885; also a pharmacist; member of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons; fellow of the American College of Surgeons; formerly city physician, health officer and county coroner; past president of the chamber of commerce; medical examiner for the draft board during World War I; served as chief surgeon at St. Christina's Hospital; for fifty years a member of the staff of the Saratoga Hospital, where he died September 12, aged 85, of hypostatic pneumonia and diabetes mellitus.

Arthur Grant Jacobs ✠ Memphis, Tenn.; University of Virginia Department of Medicine, Charlottesville, 1896; Medical College of Ohio, Cincinnati, 1897; professor of pediatrics at the University of Tennessee College of Medicine; specialist certified by the American Board of Pediatrics, Inc.; member of the American Academy of Pediatrics; chief, department of pediatrics, Baptist Memorial Hospital and the John Gaston Hospital; visiting pediatrician to the Crippled Children's Hospital School; died in the Methodist Hospital November 3, aged 69.

Stillwell Corson Burns, Philadelphia; Medico-Chirurgical College of Philadelphia, 1898; fellow of the American College of Surgeons; formerly associate professor of surgery at the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania; a major in the U. S. Army during World War I; served as surgeon in the Graduate Hospital of the University of Pennsylvania; for twenty-five years chief surgeon for the Baldwin Locomotive Works; died November 1, aged 69, of carcinoma.

Hiram Rand Corson, Issaquah, Wash.; Medical School of Maine, Portland, 1876; formerly physician to the State Soldiers' Home in Orting; died September 18, aged 95, of arteriosclerosis and mesenteric thrombosis.

Leon Charles Coté ✠ Newburgh, N. Y.; Albany Medical College, Albany, N. Y., 1917; a captain in the medical corps of the U. S. Army, serving overseas during World War I; served as president of the Newburgh Bay Medical Society; on the courtesy staff of the Highland Hospital, Beacon; on the staffs of the Wallkill State Prison Hospital, Wallkill, Cornwall Hospital, Cornwall, and the Municipal Sanatorium, Otisville; died September 27, aged 57.

Edward McClelland Cowell, Athens, Pa.; Chicago Homeopathic Medical College, 1885; a captain in the medical corps of the U. S. Army during World War I; served on the staff of the Tioga County General Hospital, Waverly, N. Y.; died in Waverly, N. Y., September 1, aged 80, of coronary occlusion.

Orlando Aaron Rogers Donnelly, Chicago; Bennett Medical College, Chicago, 1913; served as a captain in the medical corps of the U. S. Army during World War I; for many years connected with the city health department; died in the Veterans Administration Facility, Hines, September 6, aged 65, of carcinoma of the sigmoid colon.

Edwin William Dyar, Ossian, Ind.; Medical College of Indiana, Indianapolis, 1904; member of the Indiana State Medical Association; vice president and formerly president of the Ossian Bank; for many years on the staff of the Lutheran Hospital, Fort Wayne; died September 11, aged 64, of hypostatic pneumonia.

John Adair Elliott, Chicago; Jenner Medical College, Chicago, 1908; died in St. Francis Hospital, Evanston, Ill., September 26, aged 66, of bronchial asthma and myocardial insufficiency.

Evan Alexander Erwin, Laurinburg, N. C.; Medical College of the State of South Carolina, Charleston, 1912; member of the Medical Society of the State of North Carolina; secretary of the Scotland County Medical Society; served as county health officer; died September 20, aged 59, of carcinoma.

Herbert Kimball Faulkner, Keene, N. H.; Harvard Medical School, Boston, 1885; member of the New Hampshire Medical Society; formerly surgeon and trustee to the Elliot Community Hospital; served as trustee to the Keene Public Library; had been director of Faulkner and Colony Mills, the Cheshire National Bank and the New Hampshire Fire Insurance Company; died September 15, aged 85, of arteriosclerosis.

D. Harold Finch, Laramie, Wyo.; Jefferson Medical College of Philadelphia, 1917; died in Provo, Utah, September 4, aged 55, of hypertension and arteriosclerosis.

Eliezer Israel Fogel ✠ Cincinnati; Ohio-Miami Medical College of the University of Cincinnati, 1909; served during World War I; on the staff of the Jewish Hospital, where he died September 11, aged 57, of coronary occlusion.

James Lyle Fortune, Terre Haute, Ind.; Medical College of Indiana, Indianapolis, 1903; formerly county coroner; examining physician for the Redstone arsenal in Huntsville, Ala.;

examining physician for the Shriners' Hospital for Crippled Children, St. Louis; died in St. Anthony's Hospital September 26, aged 64, of cerebral hemorrhage.

Arthur Edmund Gilster ✠ Chicago; the Hahnemann Medical College and Hospital, Chicago, 1910; on the staff of the Swedish Covenant Hospital, where he died September 14, aged 57, of coronary thrombosis.

Harry E. Grishaw, Tipton, Ind.; Central College of Physicians and Surgeons, Indianapolis, 1897; member of the Indiana State Medical Association; health officer of Tipton County; on the staff of the Mercy Hospital, Elwood; died September 28, aged 71, of chronic nephritis and cardiac insufficiency.

John Edge Maines ✠ Lake Butler, Fla.; Atlanta College of Physicians and Surgeons, 1905; died August 21, aged 68, of coronary occlusion.

William Jackson Mason, Lawton, Okla.; Beaumont Hospital Medical College, St. Louis, 1894; on the staff of the Angus Hospital, where he died July 13, aged 78, of carcinoma of the liver.

Robert Keating McConeghy, Coudersport, Pa.; Jefferson Medical College of Philadelphia, 1908; past president of the Potter County Medical Society; served as coroner of Potter County for one term; on the staff of the Coudersport General Hospital; died in the Pennsylvania State Tuberculosis Sanatorium number 2, Cresson, July 27, aged 60, of pulmonary tuberculosis.

Morris Spencer McGuire, Boonville, Mo.; Missouri Medical College, St. Louis, 1895; University of Missouri School of Medicine, Columbia, 1895; on the staff of St. Joseph's Hospital, where he died August 31, aged 69, of myocarditis and angina pectoris.

William Thomas Meeks, Blairsville, Ga.; Atlanta Medical College, 1915; died July 10, aged 69, of coronary thrombosis.

Andrew Gazik Opinsky, New Kensington, Pa.; Medical College of Virginia, Richmond, 1910; member of the Medical Society of the State of Pennsylvania; contract surgeon for the U. S. Army; served as camp surgeon for the Civilian Conservation Corps camps; died July 30, aged 63, of coronary thrombosis.

James Willis Parker, Grand Blanc, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1898; a member of the board of education for many years; on the staff of the Goodrich General Hospital, Goodrich; died in Cadillac August 24, aged 72, of coronary occlusion.

MAJOR LESTER C. O'NEAL, U. S. A. (National Guard) 1906-1943

Charles Hurd Ross, Alliance, Ohio; Columbus Medical College, 1892; member of the staff of the Alliance City Hospital; died August 11, aged 76, of plasma cell myeloma.

Peter Maurice Ross, Lake Beulah, Wis.; Milwaukee Medical College, Milwaukee, 1898; served on the staffs of St. Joseph's and St. Mary's hospitals in Milwaukee; died August 24, aged 72, of coronary occlusion.

Florian A. Ruest, Pawtucket, R. I.; School of Medicine and Surgery, Faculty of Medicine of the University of Laval at Montreal, Que., Canada, 1896; member of the New England Obstetrical and Gynecological Society and the Rhode Island Medical Society; for many years health officer of Pawtucket; formerly on the staff of the Park Place Hospital; medical adviser of l'Union St. Jean Baptiste d'Amerique since 1911; died in the Memorial Hospital August 2, aged 75, of uremia.

Frank Lyon Salisbury ✠ Russellville, Ohio; Ohio State University College of Medicine, Columbus, 1917; served as a first lieutenant in the medical corps of the U. S. Army during World War I; died August 1, aged 51, of coronary thrombosis.

Howard Frederick Schultz, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1905; on the courtesy staff of the Abington Memorial Hospital, Abington, and the Hahnemann Hospital; died August 27, aged 61, of coronary thrombosis.

Claude Howard Searle, Chicago; Rush Medical College, Chicago, 1898; chairman of the board of directors since 1936 and president from 1917 to 1936 of G. D. Searle & Company; major in the medical corps of the Illinois National Guard during World War I; a founder and formerly secretary and president of the American Pharmaceutical Manufacturers Association, serving also as a member of the executive committee; died in the Evanston Hospital, Evanston, Ill., October 22, aged 71, of pneumonia.

Charles Porter Shaffer, La Verne, Calif.; St. Louis College of Physicians and Surgeons, 1892; Jefferson Medical College of Philadelphia, 1895; died August 10, aged 81, of carcinoma.

Samuel Sher, Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1907; member of the Illinois State Medical Society; served as professor of diseases of the ear, nose and throat, Post-Graduate Medical School; formerly on the staff of the Cook County Hospital; on the staffs of Grant and Edgewater hospitals and on the courtesy staff of the Wesley Memorial Hospital, where he died October 25, aged 59, of cerebral hemorrhage and arterial hypertension.

Simon Small, Boston; Tufts College Medical School, Boston, 1930; died in Lexington, Mass., July 29, aged 39.

Frederick Adams Smith ✠ Troy, N. Y.; College of Physicians and Surgeons, New York, 1891; served on the staffs of the Samaritan and the Leonard hospitals; died August 7, aged 76, of carcinoma of the adrenal gland.

Charles Ivar Spannare, Los Angeles; Bennett Medical College, Chicago, 1910; died in the Los Angeles County Hospital July 1, aged 62, of myocardial infarction and acute left ventricular failure.

William Harrold Spinks, Washington, D. C.; Washington Homeopathic Medical College, 1894; died in the Gallinger Hospital August 19, aged 68, of malignant hypernephroma of the right kidney.

Claud Milton Stewart, Lufkin, Texas; Meharry Medical College, Nashville, Tenn., 1928; died July 18, aged 46.

George W. Stratton ✠ Marysville, Calif.; Missouri Medical College, St. Louis, 1888; died August 29, aged 79.

Francis Hall Sullivan, Miami, Mo.; Marion-Sims College of Medicine, St. Louis, 1898; member of the Missouri State Medical Association; died August 14, aged 72, of cerebral hemorrhage.

James Henry Talboy, Boquette, Republic of Panama; State University of Iowa College of Medicine, Iowa City, 1884; died August 12, aged 82, of encephalomalacia.

Ralph Tousey, Seattle; Columbia University College of Physicians and Surgeons, New York, 1898; died September 25, aged 70.

Alexander Loudin Turner, Detroit; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1912; member of the Michigan State Medical Society; served on the staffs of the Grace and Woman's hospitals; died in Ravenna, Ohio, August 12, aged 61, of coronary thrombosis.

John Samuel Whitson, Enderlin, N. D.; Rush Medical College, Chicago, 1895; died August 6, aged 76, of arteriosclerosis.

Ossie Frank Wilmeth, Oakland, Calif.; Lincoln Medical College, Eclectic, Lincoln, Neb., 1916; member of the California Medical Association; died in the Providence Hospital August 26, aged 54, of coronary thrombosis.

Fredericka Caroline Zeller, Peoria, Ill.; Northwestern University Woman's Medical School, Chicago, 1894; died in the Methodist Hospital August 28, aged 80, of perforated appendicitis.

KILLED IN ACTION

Lester Cecil O'Neal ✠ Andalusia, Ala.; Louisiana State University School of Medicine, New Orleans, 1934; commissioned a captain in the U. S. Army (National Guard) on June 29, 1940; began active duty as a major on Nov. 25, 1940; killed in action in Italy Nov. 7, 1943, aged 36.

Correspondence

DISAGREEMENT ON SILICOSIS DUE TO WHEAT DUST

To the Editor:—"A Case of Silicosis Caused by Wheat Dust," by Heatley, Kahn and Rex of Toledo, Ohio, published in THE JOURNAL, April 1, is without scientific merit and should not have been accepted for publication.

A claim for silicosis compensation has been presented to the Ohio Industrial Commission on behalf of the patient whose condition is described in the article mentioned. The commissioners, who are not physicians, cannot help being impressed by the fact that a medical journal has accepted for publication an article which purports to prove that silicosis can be caused by exposure to wheat dust.

I submit some of the more obvious and significant points on which I believe the article is subject to criticism:

1. The occupational history is incomplete and does not exclude the possibility of silica exposures other than the one which is alleged by the authors.

2. The first of two x-ray films of the chest is reported to show mottling in the left lung, but there is no mention of mottling or any other type of shadow indicating parenchymatous change in the right lung. In the description of the second x-ray film, made two years later, there is no mention of any type of mottling or nodulation in either lung, nor do the published reproductions of these films show any. The only obvious findings described are in the hilar shadows and linear markings. Authorities are agreed that a diagnosis of silicosis cannot be based on exaggerated linear markings and increased hilar shadows alone, yet the authors report "a roentgenogram typical of advanced silicosis."

3. The authors give no dust counts. They state that 20 per cent of the dust analyzed was between 1 and 44 microns in particle size. They do not state how much of it was below 10 microns, which is recognized as the upper limit of size of silica particles which are capable of producing disease.

4. The dust which the authors analyzed is said to have come from a railroad car and a tunnel, but they do not state whether it came from the atmosphere breathed by the workmen or was scraped up from the floors.

5. A chemical analysis is submitted showing that this dust contained certain percentages of "silica." Chemical analysis does not distinguish between free silica and silicates. No petrographic examination or x-ray diffraction examination is reported. The authors, therefore, have not proved the presence of silicon dioxide in the dust analyzed.

6. The authors report that the second examination of the patient, after a two year interval, showed diminished vital capacity and increased emphysema, which is inferred to be the immediate cause of the patient's disability. They give no vital capacity measurements and do not mention any of the clinical or x-ray data on which their diagnosis of emphysema is based. It is the opinion of Gardner and other authorities that emphysema does not develop as a complication of silicosis until the silicosis has reached an advanced stage with extensive conglomeration of the nodular shadows.

7. The authors state that a comparison of the two x-ray films showed that "the heart shadow contour had changed as a result of the changed lung condition." They do not describe the nature of this change nor do the reproductions of the x-ray films show it. The only type of heart disease which might be induced either by emphysema or by advanced silicosis is "cor pulmonale." This is a difficult clinical diagnosis to make and probably no experienced cardiologist would attempt to make it without the help of an electrocardiogram. No electrocardiogram was reported in this case.

In conclusion, it is my contention that the authors have submitted no proof that their patient either had silicosis or had been exposed to silicon dioxide present in wheat dust.

RAYMOND C. MCKAY, M.D., Cleveland.
Member, Ohio Board of Silicosis Referees.

NOMENCLATURE OF PAPPATACI OR PAPATACI FEVER

To the Editor:—May I make a few observations regarding the paper of Sabin, Philip and Paul in THE JOURNAL, July 1, concerning the nomenclature of Papataci fever? As the authors in footnote 2 on page 603 states, the name of the vector is Phlebotomus papatasi Scolopi. P a p a = "he eats," t a s = "silently," a derivative from the Italian (see also Galli Valerio C. Bact. 0.63:226).

As can readily be seen, there is no justification for using a double p. The disease was written with a double p by the first describer (Doerr), but he stated that he used the double p for "reasons of priority," an illogical point of view, because the etymologic derivation and the name of the vector undoubtedly speak in favor of one p.

Perhaps some readers will be interested in two other synonyms of the disease. They are "soldier's fever" (because the invading Austrian troops in Bosnia were stricken but not the native population), and "dog's disease," used in Dalmatia.

DR. J. SCHWARZ, Valdivia, Chile.
Pathologist, Regional Hospital.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Narcotics: Validity of Opium Poppy Control Act as Applied to Grower of Poppy Seed for Food Purposes.—The Federal Opium Poppy Control Act of 1942 (56 Stat. 1045, 21 U. S. C. A., sec. 188 et seq.) prohibits and imposes a penalty for the production of opium poppies except when done by virtue of a license issued by the Secretary of the Treasury and defines the term "opium poppy" to include "the plant Papaver somniferum . . . and any part of any such plant." Certain growers in California of the blue seeded poppy of the species known botanically as Papaver somniferum who cultivated these poppies for their seed, an edible food product, apparently were unable to obtain a license to produce the poppy species in question for food purposes. They then brought suit in the district court, N. D. California, N. D., to enjoin the Bureau of Narcotics of the Department of the Treasury of the United States and the United States government officials charged with the enforcement of the act from interfering in any way with the growing and production of their crop of poppies. Admittedly, while the seeds of this species of poppy can be used as an edible food product, other parts of the plant are a source of opium and opium derivatives, including morphine, the fluid obtained through incisions cut in the pod yielding what is called "the raw opium." Nevertheless the growers contended that the

Opium Poppy Control Act as applied to them is unconstitutional because it is an exercise by the United States of regulatory powers over the production of an agricultural commodity, the poppy seed, within a state and that such powers are reserved exclusively to the states by the Tenth Amendment to the Constitution.

The Opium Poppy Control Act, said the district court, does not purport to regulate the production of an agricultural crop. The act is directed to the growth of opium yielding poppy plants within the United States as the source, not of an edible food product, but rather of raw opium. Its effect on the production of the poppy seed is incidental only to its operation on a plant that produces both a narcotic drug and an edible seed. The validity of the act does not depend on a finding of constitutional authority in the federal Congress to regulate a food supply but on the power of Congress to regulate the supply source of raw opium. The primary derivation of congressional authority to exercise control by federal legislation over the cultivation of the opium poppy is stated in the declared purpose of the act here in question:

> . . . (1) to discharge more effectively the obligations of the United States under the International Opium Convention of 1912, and the Convention for Limiting the Manufacture and Regulating the Distribution of Narcotic Drugs of 1931. . . .

The prime objective of the International Opium Convention of 1912 was to eradicate the opium evil and one of the methods therein agreed to to accomplish that end was through the exercise of control over the production and distribution of raw opium, defined in chapter I of the convention as:

> . . . the spontaneously coagulated sap obtained from capsules of the soporific poppy (Papaver somniferum), and which shall not have been subjected to any but the processes necessary to the packing and the transportation thereof. . . .

The later Convention for Limiting the Manufacture and Regulating the Distribution of Narcotic Drugs of 1931 (Treaty Series No. 863; 48 Stat. 1543), to which the United States was signatory, was in furtherance of the same objective as the International Opium Convention of 1912—the eradication of the drug evil, by rendering effective by international agreement the limitation of the manufacture of narcotic drugs to the world's legitimate requirements for medical and scientific purposes and by regulating their distribution. . . ."

The competence of the United States, continued the court, to enter into treaty stipulations with foreign powers designed to establish through appropriate legislation an internationally effective system of control over the production and distribution of habit forming drugs cannot be questioned, since the obligations the government there incurred were lawfully undertaken in the proper exercise of its treaty making power. And Congress is constitutionally empowered to enact whatever legislation is necessary and proper for carrying into execution the treaty making power of the United States. *Neeley* v. *Henkel,* 180 U. S. 109, 21 S. Ct. 302, 45 L. Ed. 448. By the terms of the International Opium Convention of 1912 the United States obligated itself to control the production and distribution of raw opium. The provisions of the Opium Poppy Control Act express the determination of Congress that effective control of opium production and distribution necessitates legislation limiting the proximate source of yield of the raw opium—the opium poppy—whatever the purpose for which its cultivation is undertaken.

The constitutionality of the measures thus chosen by Congress to give efficacy to the treaty stipulations of the convention is not dependent on the wisdom or success of the choice. Nor is it significant that the two conventions contain no stipulation expressly committing the signatory powers to the obligation of exercising control over the cultivation of the opium poppy. The power of Congress to enact such legislation as is necessary or proper to carry into execution powers vested by the Constitution in the United States, of which the treaty making power is one, includes the right to employ any legislative measures appropriately adapted to the effective exercise of those powers. So long as a rationally sound basis exists for the congressional determination that particular legislation is appropriately related to the discharge of constitutional powers, the validity of such legislation is unassailable.

It was apparent to the court that efficacious control over the production and distribution of raw opium can well depend on the limitation of the cultivation of the opium poppy within the United States to legitimate medical and scientific needs only. The appropriate relationship, said the court, of the means adopted by Congress to the ends thereby sought to be attained is evident. The opium poppy is the immediate source from which the raw opium is obtained; its cultivation may be undertaken without difficulty, without detection and for illicit purposes even under the guise of legitimate pretenses; the process of extracting the raw opium from the opium poppy is a simple one; the growth of the opium poppy, wherever undertaken, can reasonably be said to afford attractiveness to those seeking a source of opium supply either for the satisfaction of their own cravings or for the profits offered by the contrabrand market; and this attractiveness can be expected to increase as suppression of the drug evil becomes progressively more effective and other sources of drug supply become more scarce. In view of these considerations alone, this court is satisfied with the appropriate relativity of measures limiting the cultivation of the opium poppy to the objectives of the treaty stipulation to control the production and distribution of raw opium.

The court accordingly held that the Opium Control Act of 1942 was constitutional and denied injunctions to restrain enforcement of the Act.—*Stutz v. Bureau of Narcotics of Department of Treasury of United States; Schwein v. Same, 56 F. Supp. 810 (Calif., 1944).*

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

BOARDS OF MEDICAL EXAMINERS BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, Nov. 18, page 791.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: New York, June 8-9. Final date for filing application is March 12. Sec., Dr. George M. Lewis, 66 E. 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Feb. 19. Final date for filing application is Dec. 15. Asst. Sec., Dr. W. A. Werrell, 1301 University Ave., Madison 5, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Spring. Final date for filing application is Feb. 1. Sec., Dr. Paul C. Bucy, 912 S. Wood St., Chicago 12.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I.* Various centers, Feb. 3. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh 6.

AMERICAN BOARD OF OPHTHALMOLOGY: New York, June, Chicago, October. Final date for filing application is Dec. 1. Sec., Dr. S. Judd Beach, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF OTOLARYNGOLOGY: New York, June 5-8. Chicago, Oct. 3-6. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City, Ia.

AMERICAN BOARD OF PEDIATRICS: *Oral.* New York, April 14-15. Final date for filing application is Dec. 15. Chicago, May 19-20. Final date for filing application is Jan. 19. Sec., Dr. C. A. Aldrich, 115½ First Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* New York, June 3. Final date for filing application is May 1. Sec., Dr. B. R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1934 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American J. Obstetrics and Gynecology, St Louis

48:299-446 (Sept.) 1944. **Partial Index**

Consideration of Therapeutic Abortion. S. A. Cosgrove and Patricia A. Carter.—p. 299.
Relation of Basal Metabolic Gain During Pregnancy to Nonpregnant Basal Metabolism. L. W. Sontag, E. L. Reynolds and Virginia Torbet.—p. 315.
Measurement of Cyclic Variations in Quantity of Cervical Mucus and Its Correlation with Basal Temperature. E. Viergiver and W. T. Pommerenke.—p. 321.
Management of Delivery in Pregnancy Complicated by Serious Rheumatic Heart Disease. C. L. Mendelson.—p. 329.
Bacteriologic and Clinical Aspects of Gonorrhea in Female. A. Cohn and I. Grunstein.—p. 339.
Effect of Travel on Incidence of Abortion. A. W. Diddle.—p. 354.
Some Acquired Bony Abnormalities Influencing Conduct of Labor, with Reports of Recent Cases. A. W. Voegelin and M. L. McCall. —p. 361.
*Character of Vaginal Delivery Following Cesarean Section. Katherine Kuder and C. T. Dotter.—p. 371.
*Subclinical Postpartum Salpingitis and One Child Sterility: Pathologic Study. B. Black-Schaffer.—p. 374.
Interstitial Pregnancy: Report of Case of Full Term Gestation. M. W. Grusetz and S. H. Polayes.—p. 379.
Local Chemotherapy in Prophylaxis of Mastitis. B. R. Austin.—p. 387.
*Chorea Gravidarum: Report of Case. W. A. Ruch.—p. 392.
Pregnancy and Diabetes. A. H. Bill and F. M. Posey Jr.—p. 405.
Theca Cell Tumors of Ovary. J. L. McGoldrick and W. A. Lapp. —p. 409.

Vaginal Delivery Following Cesarean Section.—Kuder and Dotter point out that there is a difference of opinion concerning the nature of the first vaginal delivery occurring in a patient who has had a cesarean section. The question is whether or not the labor is comparable to that of a multipara or a primipara, especially in regard to the total duration of labor and the course of the first stage of labor. This study comprises a review of 34,356 pregnancies occurring in the Woman's Clinic of the New York Hospital. Of this total 496 patients had a previous cesarean section. In this group 109 patients were delivered of a full term or premature infant vaginally without ever having had a vaginal delivery preceding the first cesarean section. It was found that the average duration of labor of the first vaginal delivery in a patient who was delivered by cesarean section in her first pregnancy is identical with that in a primipara.

Postpartum Salpingitis and One Child Sterility.—Black-Schaffer presents pathologic studies consisting of bilateral tubal segments removed in the course of sterilization from 67 patients. Of this number 50 were obtained post partum following normal delivery and the remaining 17, used as controls, from patients who had undergone cesarean section. The chief indications for sterilization were, in the order of their frequency, multiparity, severe toxemias of pregnancy and heart disease. All the patients, with 1 exception, were operated on at some time between the second and the twelfth postpartum day. Bilateral tubal segments were examined microscopically. The 17 cesarean section pairs (controls) showed no pathologic lesions. Of the 50 postpartum pairs 19 were the site of a mild acute salpingitis. In no case was the salpingitis clinically recognized. It is suggested that this hitherto not demonstrated but suspected puerperal salpingitis may in some patients be the cause of tubal obstruction with resultant reduction of fertility or even sterility.

Chorea Gravidarum.—Ruch presents the history of a woman aged 20 in whom symptoms of chorea began during the second month of pregnancy. Despite rest in bed, a high vitamin diet and sedation the symptoms continued and gradually increased until, during the sixth month of pregnancy, they suddenly became quite severe. Cesarean section was performed. The contractions had practically disappeared by the time she left the hospital two weeks after operation. The appearance of the symptoms during the first trimester of pregnancy and the lack of organic disturbances seemed to rule out toxemia as the etiologic factor. The author thinks that fatigue was a strong influence and that either the attack of measles or an unsuspected mild rheumatic fever in childhood was primarily responsible. The early onset, the intermittent low grade fever and the attack of acute arthritis after recovery from the operation support this view.

American Journal of Surgery, New York

65: 303-440 (Sept.) 1944

Tumors of Urogenital Tract in the Young. C. G. Bandler and P. R. Roen.—p. 306.
*Heterogenous Skin Grafts by Coagulum Contact Method. H. I. Harris.—p. 315.
Importance of Latent Hepatic Disease. A. O. Wilensky.—p. 321.
Cryptorchidism. A. H. Iason.—p. 353.
Endocrine Factors in Mechanism of Toxemia of Pregnancy. J. Hofbauer.—p. 361.
Critical Analysis of Mammectomy and Free Transplantation of Nipple in Mammaplasty. J. W. Maliniac.—p. 364.
Ultraviolet Blood Irradiation Therapy (Knott Technic) in Nonhealing Wounds. G. Miley.—p. 368.
Use of Foreign Body Locator (Berman) in Industrial Practice. M. Parkes.—p. 373.
Treatment of Inflammatory Urethral Strictures. R. Lich Jr.—p. 381.
Pilonidal Sinuses and Cysts: Recommended Method of Treatment. P. Peterson and R. H. Ames.—p. 384.
*Use of Tyrothricin in Treatment of Ulcers of Skin. L. M. Rankin. —p. 391.
Sulfonamides in Appendicitis: Review of 412 Consecutive Cases and Analysis of Fatalities. L. R. Kaufman and W. L. Mersheimer. —p. 393.
Gastric Lesions High on Lesser Curvature. M. S. Rosenblatt.—p. 404.
Treatment of Fractures: Application of Principle of Rest. M. M. Simon.—p. 406.

Heterogenous Skin Grafts by Coagulum Contact Method.—Harris reports that a girl aged 12, one side of whose body, including the entire upper and lower extremity, had been burned completely, was in an extremely poor condition after four months of ineffective treatment. Since she had no skin to spare, a graft was taken from her father. The results of the grafting were excellent; the take was perfect. The only objectionable feature was the fact that blood had to be taken from the patient, and this she resented because of the pain, so that the author was hesitant to take even 20 cc. of blood for another graft. At a second graft it was decided to use the plasma and cell extract, as well as the skin, from the father. The procedure was done and two drums full of skin, the same size as the first one (10 by 15 cm.), were taken and applied to the pelvis and buttock. These grafts also showed a complete take. Since the father could not donate any more skin, it was decided to try a heterogenous isograft with a stock blood plasma and cell extract. The results of this also were excellent. The author reports 8 other cases. Sano removes the graft and places it on a piece of gauze and then paints on the cell extract. The author paints the cell extract on the graft while it is still on the drum, when the Padgett machines are used. Painting the cell extract on the graft while still on the drum might be advantageous because the fluid has a better opportunity to fill all the interstices. After it is removed from the drum the graft shrinks, but the entire surface of the graft will have been covered, with the result that it has a better chance of agglutinating to the entire surface. Complete hemostasis must be accomplished in all cases before the grafts are applied.

Tyrothricin in Ulcers of Skin.—Rankin describes 6 cases of old chronic ulcers in which tyrothricin was used. Tyrothricin consists of gramicidin and tyrocidine. Reports show that it is of value in the treatment of mastoiditis, empyema, suppurating arthritis and deep wound infections. While investigators mention the action of tyrothricin on the bacteria in the ulcer, no mention has been made of one property that the author noticed in 5 of the 6 patients treated, namely tissue stimulation. Tyrothricin did not cause toxic symptoms in the 6 patients; it was a

good antibactericidal agent when applied locally; it caused no pain or discomfort when used locally in the proportion of 0.25 cc. to 99.75 cc. of water. Excellent results were obtained in 5 of the 6 patients.

American Review of Tuberculosis, New York

50:185-266 (Sept.) 1944

Evolution of Rest Treatment of Pulmonary Tuberculosis. J. H. Pratt.—p. 185.
Evaluation of Chemotherapeutic Agents in Clinical Tuberculosis: Suggested Procedure. H. C. Hinshaw and W. H. Feldman.—p. 202.
Mass Chest Roentgenography and Admissions to Olive View Sanatorium. J. Goorwitch.—p. 214.
Basal Metabolism in Pulmonary Tuberculosis. G. C. Leiner.—p. 223.
Nutritional Studies in Tuberculosis: III. Thiamine (Vitamin B_1) Deficiency and Peripheral Neuritis. J. E. Farber and D. K. Miller. —p. 229.
Cardiorespiratory Testing in Tuberculosis: Preliminary Report. K. A. Harden, H. M. Payne, Maurine P. Weaver and J. R. Laurey. —p. 234.
Tomorrow's Tuberculosis Associations. W. P. Shepard.—p. 244.
Perspectives and Trends in Tuberculosis. H. S. Willis.—p. 251.

Anesthesiology, New York

5:441-550 (Sept.) 1944

Undergraduate Medical Education and Anesthesiology. R. B. Allen. —p. 441.
Benefits and Hazards of Pentothal Anesthesia. K. M. Heard.—p. 448.
Continuous Drop Method for Subarachnoid Analgesia: Preliminary Report. Julia G. Arrowood and F. F. Foldes.—p. 465.
Some General Considerations in Evaluating Local Anesthetic Solutions in Patients. M. L. Tainter and L. Winter.—p. 470.
Stellate Ganglion Block: Definite Anterolateral Approach. P. P. Volpitto and W. A. Risteen.—p. 491.
Anesthesia: XIV. Study of Certain Physical Properties of Isopropenyl Vinyl Ether. C. J. Carr, Dorothy Kibler and J. C. Krantz Jr.—p. 495.
Intercostal Block with Long Acting Anesthetic in Upper Abdominal Operations. S. Belinkoff.—p. 500.
New Concepts of Morphine Analgesia. D. Slaughter.—p. 508.
Experiences with Pentothal Sodium Anesthesia in War Casualties. S. L. Lieberman.—p. 517.

Annals of Internal Medicine, Lancaster, Pa.

21:367-564 (Sept.) 1944

Traumatic Neuroses in Court. H. W. Smith and H. C. Solomon. —p. 367.
Dietary Factor in Etiology of Pernicious Anemia. J. M. Askey. —p. 402.
Psychotherapy. S. Katzenelbogen.—p. 412.
*Impending Myocardial Infarction. L. Waitzkin.—p. 421.
Clinicopathologic Study of 100 Cases of Acute and Chronic Gallbladder Disease. W. Johnson, B. E. Malstrom and B. W. Volk. —p. 431.
Subclinical Vitamin Deficiency: V. Assay of Subclinical Thiamine Deficiency. Mildred Carleen Hulse, N. Weissman, E. Stotz, M. Clinton and J. W. Ferrebee.—p. 440.
Hemoptysis in Tuberculosis, with Differential Discussion of Other Causes. L. J. Moorman.—p. 447.
Direct Measurements of Effects of Bromides, Sodium Amytal and of Caffeine in Man. E. Jacobson.—p. 455.
*Some Clinical Characteristics of Mumps, and Effect of Belladonna in Treatment: Study Made at Station Hospital, Fort George G. Meade, Maryland. H. W. Potter and L. H. Bronstein.—p. 469.

Impending Myocardial Infarction.—According to Waitzkin, acute myocardial infarction is preceded by premonitory symptoms in a considerable percentage of cases. He found that of 61 consecutive cases of acute infarction treated in the past two years 17 showed premonitory symptoms. The symptoms have the following characteristics: 1. There may be one or more episodes of spontaneous prolonged cardiac pain, mild or severe, with or without a preceding history of coronary artery disease. 2. Cardiac pain of short duration, on customary or no exertion, suddenly appears where none existed before. 3. In patients with preexisting angina pectoris, cardiac pain appears on rapidly decreasing amounts of exertion or at rest. In considering symptoms suspected as premonitory, it must be recognized that myocardial infarction does not inevitably follow them; but the strong possibility that it may should lead to suspicion and therapeutic precautions.

Clinical Characteristics of Mumps, and Effect of Belladonna in Treatment.—Potter and Bronstein review 124 cases of mumps. This study was originally undertaken in an effort to ascertain the value of treating such patients with belladonna. The use of this drug had been suggested to shorten the course of the disease and to decrease the incidence of complications. On admission the soldier was given 1/100 grain (0.65 mg.) of atropine sulfate and then 1 cc. of the tincture of belladonna by mouth every two hours, until atropinization, as evidenced by dilatation of the pupil and/or dryness of the throat, was produced. Subsequent medication was given in doses to keep these changes constant, either until the patient was cured or until gastrointestinal discomfort made it necessary to discontinue the drug. Belladonna was used in treating 42 of these cases without any effect on the duration of illness, incidence of complications, duration of orchitis or comfort of the patient. The distinction between rural and urban origin of the soldier is no longer as definite as it was in previously reported series of cases, probably because of decreased isolation of population groups. Most of the men developed mumps within their first year of service and possible exposure and not in the first two months as reported in the first world war. Early hospitalization does not shorten the duration of the disease.

Archives of Dermatology and Syphilology, Chicago

50:151-230 (Sept.) 1944

Erysipelothrix Rhusiopathiae Infection in Swine and in Human Beings: Comparative Study of Cutaneous Lesions. J. V. Klauder.—p. 151.
Clinical Manifestations of Vitamin Deficiencies as Observed in Federated Malay States. P. Fasal.—p. 160.
Epidermolysis Bullosa. J. L. Mooney.—p. 167.
*Dermatophytosis in Industry. S. M. Peck, I. Botvinick and L. Schwartz.—p. 170.
Multiple Painful and Painless Glomus Tumors. A. H. Slepyan.—p. 179.
Connective Tissue Nevus. K. Steiner.—p. 183.
*Dyskeratosis Congenita with Pigmentation, Dystrophia Unguium and Leukoplakia Oris (Cole and Others): Report of Cases of 2 Brothers, with Improvement in Leukoplakic Patches in 1 with Androgenic Medication. J. Garb and G. Rubin.—p. 191.
*Early Syphilis Masked and Delayed by Penicillin in Treatment of Gonorrhea. Bertha Shafer and S. J. Zakon.—p. 200.

Dermatophytosis in Industry.—Peck and his associates examined for dermatophytosis 2,123 workers in two munitions plants, three plants processing steel and other metal parts and one plant making glass products. Two of the plants were revisited at different seasons. On clinical grounds alone results for the 2,123 workers were classified as 27.79 per cent positive, 33.63 per cent doubtful and 38.57 per cent negative. Cultural studies revealed that some patients in the clinically doubtful group had true dermatophytosis. There was no significant difference in sex incidence. When the personnel of the same plants was examined at different seasons, the number of clinically negative workers rose from 13 to 19 per cent in the summer to 54 per cent in the winter. Trichophyton gypseum was the pathogenic fungus most often recovered, Trichophyton purpureum was next in frequency and Trichophyton inguinale was recovered from 1 case. All of the cultures of T. purpureum were recovered in one locality. Shower room flooring of concrete or pine wood is a possible but not likely source of fungous infections of the feet. Copper impregnated concrete flooring was found to be of no value in the prevention of the spread of fungous infections of the feet. Trichophytin tests were made on 776 workers. Of these 42.53 per cent had positive reactions. Of the 558 men tested, 52 per cent had positive trichophytin tests; of 218 women tested, 29.96 per cent had positive trichophytin tests. Lower incidence in women of a demonstrable allergy to fungi and/or their products may explain why women are less affected by dermatophytosis of the feet than are men, since it may be responsible for less subjective symptoms. The trichophytin test is more often positive in patients with clinically active dermatophytosis of the feet than in those showing no evidence of the disease. There is no indication that the presence of an allergy to fungi and/or their products bears any relationship to the acquisition of an allergic contact dermatitis. Dermatophytosis and its allergic manifestations are not important factors in lost time among industrial workers.

Dyskeratosis Congenita, Dystrophia Unguium and Leukoplakia Oris.—Garb and Rubin report the histories of 2 brothers with dyskeratosis congenita with pigmentation, dystrophia unguium and leukoplakia oris, a rare dermatosis. This syndrome has been described by Cole, Rauschkolb and Toomey, who reported 1 case and discussed 2 which had been observed by Engman. All 5 cases have in common pigmentation, leukoplakia oris and dystrophy of the finger nails and toe nails. They also have a change in the skin of the hands resembling acroder-

matitis chronica atrophicans. The cases seen by the authors differed from those of Cole, Rauschkolb and Toomey and Engman in the character of pigmentation, which consisted of rhomboid-like purplish spaces enclosing normal skin, in contrast to the whitish raised papules with a fine reddish base in the patient of Cole and his associates and to the 1 mm. spots surrounded by pigment arrayed in a peculiar network in Engman's case. The lesions of the mouth and the nails were similar to those of the other 3 cases except that the leukoplakic lesions in the older brother were more extensive and were complicated by bullae and ulcerations of the commissures of the lips. His nails were more dystrophic than those of his younger brother and the other 3 patients. The brothers had additional features, the most important being mental retardation. There was evidence of vitamin B complex deficiency in all 5 cases so far reported. This was manifested chiefly by leukoplakia, dystrophy of the nails and in the first of the reported cases by intestinal hypomotility. This patient was treated at first with testosterone propionate, to which the leukoplakic patches responded well, undergoing pronounced regression in three weeks, and recently with large doses of vitamin B complex.

Early Syphilis Masked by Penicillin Used for Gonorrhea.—Shafer and Zakon point out that penicillin is the first therapeutic agent to be effective in the treatment of both gonorrhea and syphilis. However, the difference in the apparently curative doses of penicillin in the treatment of these two diseases presents a grave problem in that early syphilis may be masked and delayed by the use of doses of penicillin which are curative for gonorrhea but which are totally inadequate for syphilis. This problem is illustrated with a case report.

Archives of Surgery, Chicago

49:75-146 (Aug.) 1944

Treatment of Rhinorrhea and Otorrhea. W. E. Dandy.—p. 75.
*Plasma Cell Mastitis: Report of 5 Additional Cases. W. H. Parsons, J. C. Henthorne and R. L. Clark Jr.—p. 86.
Roentgen Features of Chronic Tuberculous Peritonitis. J. J. McCort.—p. 91.
Effect of Massive Experimental Hemorrhage on Hepatic Function in Dogs. C. Ireneus Jr. and C. R. Puestow.—p. 100.
*Aseptic Necrosis of Head of Femur Following Traumatic Dislocation of Hip. S. Kleinberg.—p. 104.
Review of Urologic Surgery. A. J. Scholl and others.—p. 109.

Plasma Cell Mastitis.—Plasma cell mastitis of Adair is a relatively uncommon disease. It is important because of its clinical resemblance to carcinoma of the breast. The resemblance is so close that in at least half of the recorded cases primary radical mastectomy was performed on the assumption that the condition was malignant. The 5 specimens reported in this communication were collected by Parsons and his collaborators from a total of 1,500 specimens from female breasts studied during the past six and a half years from the services of the Vicksburg Hospital and from other sources in Mississippi. The clinical features of these cases duplicate those common to most of the other recorded cases. In case 1 the resemblance to carcinoma of the breast was embarrassingly close. In case 2 the lesion was more suggestive of an inflammatory process, although it was only moderately tender, and the nipple was retracted. Some features of this disease have not been reported before, including recurrence of the lesion, which was observed in cases 2 and 3, and diffuse comedomastitis, which coexisted in portions of the mammary glands in cases 1 and 5. In case 2 the tonsils were badly diseased and the speculation is advanced that the focal infection may have contributed to the development of the mastitis, because in another case of indolent mastitis trouble with the breast continued until tonsillectomy was carried out, after which, without other therapy, the mastitis promptly subsided. The first patient went through a normal pregnancy in the same year in which her breast was removed without the development of mastitis in the remaining breast. The second patient had been castrated five years before the onset of symptoms referable to the breast and the course of the plasma cell mastitis covered three years, which is an unusually prolonged time for this condition. The apparent difference in the endocrine constitution in the 2 cases seems worthy of comment. The condition is a periductal inflammatory reaction caused by extravasation of material from the ducts into the periductal fibrous tissue and is a true clinical entity.

Aseptic Necrosis of Head of Femur.—Kleinberg calls attention to the possibility of traumatic dislocation of the hip occurring without rupture of the ligamentum teres. He reports a typical case of aseptic necrosis and deformity of the head of the femur with its ligamentum teres intact and thoroughly vascularized, the pathologic condition having arisen from a traumatic interruption of the blood supply of the femoral head coming through the capsule of the hip joint. From experience in operations on the hip joint in which the femoral head is deliberately dislocated from the acetabulum the author has learned that, whereas most of the time the ligament is torn, if manipulations have not been sudden or violent the head can be pried out of the acetabulum without rupturing the ligament. It is possible, therefore, to visualize a traumatic dislocation of the hip without rupture of the ligamentum teres. That must have been true in the case here reported. The force producing the dislocation tore the capsule and its blood vessels, thereby depriving the femoral head of a large source of its blood supply. As a result there ensued an aseptic necrosis with collapse of the bony structure arising from too early weight bearing. One might assume that the ligamentum teres had been torn but that the fragments had fortuitously come accurately and intimately in contact after the reduction and had reunited. But in such an event, which is extremely unlikely, there would remain some scars of healing, and none were visible. The normal ligamentum teres in the reported case proves that rupture of the ligament is not a constant occurrence in a traumatic dislocation and that typical aseptic necrosis of the femoral head may occur even though its blood supply through the ligamentum teres has not been disturbed.

Arizona Medicine, Phoenix

1:165-228 (July) 1944

Peptic Ulcer. P. J. Cunnane.—p. 183.
X-ray Findings in Silicosis: Supplementary Report of Subcommittee on Industrial Health, Arizona State Medical Association. W. W. Watkins.—p. 187.
Vital Capacity in Silicosis. W. L. Minear.—p. 190.
*Sulfonamides in Treatment of Chronic Bronchial Infections. W. H. Oatway, Jr.—p. 194.
Peptogenic Ulcer in Meckel's Diverticulum: Case Report. Z. B. Noon.—p. 197.
Cystic Diseases of Lung. E. C. Reed.—p. 200.

Sulfonamides in Chronic Bronchial Infections.—The report is concerned with the use of sulfadiazine, sulfamerazine and sulfathiazole in 48 cases with purulent bronchial secretion. The diagnosis was chronic bronchitis in 11 cases, bronchial asthma with bronchitis in 11 cases and bronchiectasis in 16 cases. The author is concerned chiefly with the 16 cases of bronchiectasis. The symptoms had persisted for from one to twenty-five years. The daily volume of sputum varied between 20 and 800 cc. Administration of sulfonamides by mouth has been found regularly effective in all cases of simple, uncomplicated bronchiectasis. The sputum was reduced in all cases. The average was a 62 per cent decrease. In the presence of atelectasis and putrid secretions the sulfonamides were much less efficient than in simple bronchiectasis. Tolerance has been about as expected except in cases known to be clinically allergic. There is no reason to believe that the lesion structure of bronchiectasis will change, though progress may be prevented by sulfonamide treatment. It is recommended that sulfonamides be used in nonsurgical cases and for preoperative therapy. It should be combined with postural drainage, bronchoscopic aspiration, climatotherapy and treatment of the sinuses.

Bulletin of Johns Hopkins Hospital, Baltimore

75:1-72 (July) 1944

Comparison of Bacteriostatic Activities of Some of Newer Sulfonamide Compounds. Eleanor A. Bliss and Helen C. Deitz.—p. 1.
Experimental Shock: II. Effects of Acute Plasmapheresis in Healthy Dogs. P. B. Price, W. Metcalf, W. P. Longmire, C. R. Hanlon and H. V. Rizzoli.—p. 14.
Tryptophan Derivatives in Urine of Pyridoxine Deficient Swine. G. E. Cartwright, M. M. Wintrobe, Patricia Jones, Marjorie Lauritsen and S. Humphreys.—p. 35.
Diagnosis of Influenza Virus Infections by Agglutination-Inhibition Test. T. W. Farmer and G. A. Streeter, with technical assistance of Helen C. Deitz.—p. 48.
Cold Hemagglutination in Primary Atypical Pneumonia. G. A. Streeter, T. W. Farmer and G. S. Hayes.—p. 60.

Canadian Medical Association Journal, Montreal

51:195-292 (Sept.) 1944

Returning Serviceman and His Problems. J. C. Meakins.—p. 195.
Reintegration of War Veteran in Industry. D. E. Cameron.—p. 202.
*Intravenous Pectin Solution in Prophylaxis and Treatment of Shock. R. D. McClure, K. W. Warren and L. S. Fallis.—p. 206.
*Results of Surgical Treatment of Sciatica Due to Herniation of Intervertebral Disk in Canadian Soldiers Overseas. E. H. Botterell, W. S. Keith and O. W. Stewart.—p. 210.
Sulfadiazine Prophylaxis in Nasopharyngitis and Scarlet Fever. J. D. Keith, A. Ross and R. K. Thomson.—p. 214.
Theoretical and Experimental Aspects of Surgical Refrigeration. F. M. Allen.—p. 220.
General Practice: A Specialty. J. L. Little.—p. 227.
*Absorption of Sulfathiazole from Wounds. R. A. Waud.—p. 229.
Some Distinctions Between Health Services and Care of Sick. H. Emerson.—p. 234.
Cold Agglutinins and Pneumonias. C. B. Rich, M. V. Rae and C. J. McGoey.—p. 239.
Sudden Deafness. A. L. Yates.—p. 240.
Sulfonamides and Acute Ear Infections. H. W. Schwartz.—p. 245.
Miscellany of Anesthesia Bugbears. G. D. Stanley.—p. 249.
Symmetrical Lividity of Soles. F. Kalz and Helen Friedman.—p. 252.
External Abdominal Hernia. F. W. Schroeder.—p. 253.
Gonorrheal Iridocyclitis Treated by Penicillin, with Report of Case. A. J. Elliot.—p. 257.
Carcinoid Tumor of Ileum with Metastases in Mesenteric Lymph Nodes. W. O. Stevenson and A. J. Blanchard.—p. 259.

Intravenous Pectin Solution in Shock.—McClure and his associates report experiences with pectin solution in treating 275 patients who received the solution prophylactically during some major surgical procedure on the gastrointestinal tract. There were 6 total gastrectomies, 85 partial gastrectomies, 2 pancreatectomies, 1 colectomy, 11 abdominoperineal resections of the rectum, 14 anterior resections of the rectum and 11 Mickulicz and 12 primary resections of the colon. The remaining cases included 11 radical mastectomies, 11 neurosurgical procedures, 19 operations on traumatic and postoperative shock victims, 14 biliary tract operations and 69 miscellaneous operations. All pectin solutions were prepared by Hartman and Schelling, who emphasize the care which must be observed in the preparation and standardization of pectin solutions. Each batch must be tested separately for its osmotic pressure, viscosity and specific gravity. The p_H must be adjusted carefully to 7.0. In most instances pectin solution was administered as a single infusion concurrent with the operation. In a few cases it was given in two divided doses. The amount varied between 200 and 1,600 cc. of 1 per cent solution, the most frequent dose being 800 cc. The authors conclude that pectin, though inferior to blood or plasma, appears to be of more value than glucose or saline solution in the prophylaxis of shock in extensive surgical procedures. Pectin is nontoxic and nonantigenic in the quantity of 1,000 to 1,500 cc. usually required to maintain blood pressure in the presence of shock producing conditions. Untoward results appeared only after the intravenous injection of amounts in excess of 4,000 cc.

Surgical Treatment of Sciatica Due to Herniation of Intervertebral Disk.—Botterell and his associates begin with a period of conservative treatment, with complete rest in bed for three weeks. If there is no improvement or if the improvement is short of enabling patients to reengage in their former duties or duties of a less strenuous character, operation may then be considered expedient. A longer period of rest in bed may be prescribed before any decision to operate is made if the improvement is moderate and continuing. Operation is not undertaken, however, if there are any other physical defects or unstable emotional or mental reactions which would make doubtful return to duty following operation. The exceptions to this policy are those whose pain is unusually severe and is not relieved by bed rest alone and those for whom operation is done to stop the rapid progression of muscular atrophy and patients with paresis of the bladder or bowel. Following operation the patient is kept in bed for from two to three weeks. His reconditioning begins in the form of tension exercises during the last few days in bed. A few days later restricted physical exercises are started and he progresses through an increasing range of activity. Fifty-one Canadian soldiers have been studied since operation. Twenty-nine have returned to full duty and 14 to sedentary duty. Eight were unfit for military duties.

Absorption of Sulfathiazole from Wounds.—Waud aimed to determine the rate and depth of diffusion of sulfathiazole into the underlying tissue when applied to wounds. The influence of various bases (water miscible and fatty) on diffusion into the tissues also was studied. Rabbits were used in all experiments. Estimations of the concentration of sulfathiazole were made at different levels below the floor of the wounds and at different periods following the application of different concentrations of the drug. It was found that the higher the percentage of the drug in the base the greater was the concentration obtained in the tissues. The concentration obtained in tissues beyond 2 to 3 mm. below the surface of the wound is much less than that ordinarily reached when sulfathiazole is given by mouth. This may not be sufficient to prevent the spread of infection and may justify the systemic administration of the drug. The level of sulfathiazole obtained in the blood when the drug is applied locally approximates that of the tissues situated at a level anywhere between 3 and 7 mm. below the surface of the wound. The delivery of sulfathiazole out of a water soluble base or an oil in water emulsion takes place quite readily. When incorporated in a fatty or paraffin base and applied to an open wound, little of the drug reaches the tissues. When suspended in a liquid oil, the sulfonamide falls out and is deposited in almost the pure state on the surface of the wound or dressing.

Cancer Research, Baltimore

4:529-600 (Sept.) 1944

Chromosome Size in Normal Rat Organs in Relation to B Vitamins, Ribonucleic Acid and Nuclear Volume. J. J. Biesele.—p. 529.
Size and Synthetic Activity of Chromosomes of Two Rat Neoplasms. J. J. Biesele.—p. 540.
Comparative Glycolytic and Respiratory Metabolism of Homologous Normal, Benign and Malignant Rabbit Tissues, with Particular Reference to Benign Virus Papilloma (Shope) and Transplanted Cancer Derived Therefrom (the V 2 Carcinoma). J. G. Kidd, R. J. Winzler and D. Burk.—p. 547.
Multiple Primary Malignant Tumors and Susceptibility to Cancer. S. Warren and T. Ehrenreich.—p. 554.
Cancer of Liver in Negro in Africa and in America. E. L. Kennaway. —p. 571
Observations on Mouse Tumors Cultivated in Yolk Sac of Embryonic Chick. F. R. Heilman and J. J. Bittner.—p. 578.

Endocrinology, Springfield, Ill.

35:139-228 (Sept.) 1944

Effect of Stilbestrol on Experimental Streptococcal Infection in Mice. G. E. Foley and W. L. Aycock.—p. 139
Pituitary Responses of Mature Male Rats to Oxidative Inactivation Product of Estrone. O. W. Smith.—p. 146.
Thyroid and Metathyroid Diabetes. B. A. Houssay.—p. 158.
Influence of Reproductive Hormones on Growth in Ovariectomized and Normal Female Rats. R. Bogart, J. F. Lasley and D. T. Mayer. —p. 173.
Testicular Response to Androgen in Light Stimulated Starling. J. W. Burger.—p. 182.
Effect of Thiamine Deficiency and Controlled Inanition on Ovarian Function. V. A. Drill and Marie W. Burrill.—p. 187.

Florida Medical Association Journal, Jacksonville

31: 41-84 (Aug.) 1944

Torsion of Omentum. R. R. Killinger.—p. 61.
Guillain-Barré Syndrome: Brief Review of Literature and Presentation of Case. S. Wright and J. Jewett.—p. 64

31: 85-128 (Sept.) 1944

Primary Atypical Pneumonia: Analysis of 140 Cases. M. B. Guthrie and R. Reeser Jr.—p. 101.
Pulmonary Congestion and Edema in Cardiac Failure. W. C. Blake. —p. 104.

Illinois Medical Journal, Chicago

86:81-128 (Aug.) 1944

Test of Labor W. C. Danforth.—p. 90.
Reconditioning Program for Disabled Soldiers. H. C. Lueth.—p. 93.
Filariasis: Public Health Aspects and Prognosis. J. W. Firoved.—p. 97.
Diagnosis and Treatment of Anorectal Diseases in Station Hospital. E. H. Quandt.—p. 99.
Responsibility of Physician in Industrial Practice. C. D. Selby.—p. 117.

86:129-180 (Sept.) 1944

Care of Cleft Lip and Palate in Babies. L. W. Schultz.—p. 138.
Treatment of Varicosities Involving Internal Saphenous Vein. J. T. Gault.—p. 159.
Colic Due to Crystalluria. S. W. Raymond.—p. 162.
Medical Management of Jaundice. F. Steigmann and H. Popper.—p. 164.
Recent Data on Health Hazards in War Industries. W. J. McConnell. —p. 170.

Journal of Clin. Endocrinology, Springfield, Ill.

4:287-356 (July) 1944

*Pork Adrenal Cortex Extract: Effect on Carbohydrate Metabolism and Work Capacity in Addison's Disease. C. M. MacBryde and F. A. de la Balze.—p. 287.
Growth and Treatment of Dwarfs and Giants. Leona M. Bayer.—p. 297.
Sexual Infantilism in Females: Causes, Diagnosis and Treatment. L. Wilkins and W. Fleischmann.—p. 306.
Perlingual Absorption of Progesterone and Anhydrohydroxyprogesterone: II. Clinical Evaluation. R. B. Greenblatt.—p. 321.
Evaluation of Method for Measuring and Survey of Urinary Excretion of Weakly Phenolic Ketone "Estrone" in Endocrine Disorders. E. C. Reifenstein Jr. and Eleanor F. Dempsey.—p. 326.
Embryology of Sexual Structure and Hermaphroditism. R. R. Greene. —p. 335.

Pork Adrenal Cortex Extract in Addison's Disease.—MacBryde and de la Balze describe studies with pork adrenal cortex extract for Addison's disease. This extract has for the first time provided a means of restoring the carbohydrate metabolism to normal. The authors made studies on 7 patients with Addison's disease, which reveal that pork adrenal cortex extract has a direct action on carbohydrate metabolism and that this action is greater than that of beef adrenal cortex extract. One cc. of the pork extract (in oil) represents approximately the same survival growth potency (40 rat units) as 10 cc. of beef extract (aqueous). When given intramuscularly in these proportions, usually in doses of 2 cc. and 20 cc. respectively, the pork extract tends to correct the blood sugar abnormalities of Addison's disease, while beef extract exerts comparatively little such effect. In 7 patients with Addison's disease the pork adrenal cortex extract produced (1) increased absorption of glucose from the gastrointestinal tract, (2) prevention of hypoglycemia after food or glucose intake or as the result of prolonged fasting (this apparently is accomplished by increasing the glucose output from the liver), (3) increased utilization of glucose by the tissues as indicated by higher capillary and lower venous blood sugar and greater arteriovenous differences, (4) increased muscular work capacity and (5) adequate control of salt and water metabolism as well as of carbohydrate metabolism when given in small doses daily. The greater proportional effect of pork adrenal cortex extract is apparently due to its higher content of the steroids, having an O or OH on C_{11}, such as corticosterone and 17-hydroxy-11-dehydrocorticosterone (Kendall's compound E). The extract seems not only to mobilize glycogen from the liver but also to increase the utilization of glucose by the muscles. This is contradictory to the conclusions of some workers who have interpreted the higher blood sugars produced in animals by cortex extracts as evidence of decreased carbohydrate oxidation. The results obtained by the authors favor these conclusions: Rather than exerting antiinsulin activity, physiologic amounts of the cortical carbohydrate hormone work synergistically with insulin to promote carbohydrate utilization; the cortical hormone causes release of glucose from the liver; the higher blood sugar then causes increased insulin secretion, which results in greater arteriovenous difference in the blood sugar in consequence of greater utilization by the muscles.

Journal of Immunology, Baltimore

49:129-192 (Sept.) 1944

Sulfathiazole-Acetaldehyde Sodium Bisulfite in Experimental Group C Streptococcal Infections. E. J. Foley, Jeanne A. Epstein and S. W. Lee.—p. 129.
Semliki Forest Virus: I. Isolation and Pathogenic Properties. K. C. Smithburn and A. J. Haddow.—p. 141.
Id.: II. Immunologic Studies with Specific Antiviral Sera and Sera from Humans and Wild Animals. K. C. Smithburn, A. F. Mahaffy and A. J. Haddow.—p. 159.
Influence of Age on Susceptibility of Mice to Infection with Certain Neurotropic Viruses. E. H. Lennette and H. Koprowski.—p. 175.

Journal of Nervous and Mental Disease, New York

100:229-342 (Sept.) 1944

Studies on Virus Nature of Infectious Agent Obtained from Four Strains of "Neurotropic" Alpha Streptococci. E. C. Rosenow.—p. 229.
Principle of Compensation of Nervous Function. W. Riese.—p. 263.
Alterations in Structure of Motor Nerve Endings in Skeletal Muscle of Rabbits. W. B. Dublin.—p. 275.
Sleep Paralysis, with Report of 2 Cases. P. Chodoff.—p. 278.
Indexing of Psychiatric Records for Clinical Use and Research. E. J. Doty.—p. 282.
Personality Changes Characterizing Transition from Civilian to Military Life. G. Bychowski.—p. 289.

Medicine, Baltimore

23:215-280 (Sept.) 1944

Hemoglobin, Plasma Protein and Cell Protein: Their Interchange and Construction in Emergencies. G. H. Whipple and S. C. Madden. —p. 215.
*Pathogenesis of Cushing's Syndrome. P. Heinbecker.—p. 225.
Aerobic Nonhemolytic Streptococci: Critical Review of Their Characteristics and Pathogenicity, with Special Reference to Human Mouth and to Subacute Bacterial Endocarditis. T. Rosebury.—p. 249.

Pathogenesis of Cushing's Syndrome.—Heinbecker presents clinical studies in 6 cases of Cushing's syndrome as well as experiments on dogs. In 5 of the cases the hypothalamus was available for study. Hyalinization of basophil cells was found in all 5. In 4 changes in the hypothalamic nuclei, particularly the paraventricular nuclei, were noted. In none of these 4 was an adrenal tumor present. In the fifth case, in which a malignant adrenal tumor was found at necropsy, no hypothalamic lesion was present. In the sixth case an adrenal tumor was removed at operation but the brain was not available for study. Dogs with an experimental lesion of the hypothalamus involving areas similar to those found involved in 4 cases exhibiting Cushing's syndrome show definite loss of basophil cells, with degenerative changes in the remaining basophil cells in the hypophysis. In such animals changes occur in the thyroid, in the gonads and in the islets of the pancreas of a type which serves to explain many of the symptoms of Cushing's syndrome. Experimental evidence is offered to show that at least two of the primary lesions could be expected to cause a disturbance of lipid metabolism characterized by an accumulation of fat and cholesterol in the adipose tissue of certain regions of the body. In dogs with complete or partial bilateral destruction of the caudal portions of the paraventricular nuclei there is just such an infiltration of fat and cholesterol into tissues such as the skin, the muscles, the liver and the walls of the blood vessels as occurs in persons exhibiting Cushing's syndrome. The author thinks that the conclusion now seems permissible that either an adrenal tumor or hypofunction of the paraventricular hypothalamic nuclei may be primary causes of the basophil degeneration which in turn is the immediate cause of many of the typical findings of Cushing's syndrome. Evidence is presented to suggest that the hypothalamic dysfunction may lead to hyalinization of the basophil cells through an increased effectiveness of the hormone secreted by the adrenal cortex. In this way a common pathway for influencing the hypophysis is found for the various primary disturbances which lead to Cushing's syndrome.

New England Journal of Medicine, Boston

231:243-376 (Sept. 7) 1944

*Paget's Disease: Its Pathologic Physiology and Importance of This in Complications Arising from Fracture and Immobilization. E. C. Reifenstein Jr. and F. Albright.—p. 343.
Eosinophilic Infiltration of Lungs (Loeffler's Syndrome). S. H. Jones and C. R. Souders.—p. 356.
Penicillin Sodium Therapy in Experimental Weil's Disease. D. L. Augustine, D. Weinman and Joan McAllister.—p. 358.
Thoracic Surgery. J. W. Strieder.—p. 360.

Paget's Disease.—Reifenstein and Albright call attention to the occurrence of acute atrophy of bone as a complication of Paget's disease. The bone lesions of Paget's disease are not generalized but spotty in their distribution. This fact alone is strong evidence against the disturbance being on an endocrinologic or metabolic basis. The initial lesion of Paget's disease is bone destruction, the cause of this being entirely obscure. The resultant weakness of the involved bones renders them less resistant to stresses and strains, and this leads to a stimulation of the osteoblasts and an overproduction of bone. In the skull, where there are fewer stresses and strains, one frequently encounters bone destruction divorced from the overproduction of bone (so-called acute Paget's disease of the skull). The repair of bone by the osteoblasts is never completed, since the localized initial disorder causing bone destruction apparently persists. There results alternating destruction and repair of bone, which eventually leads to the pathognomonic "mosaic structure." This mosaic appearance is due to the irregular cement lines, each one of which demarcates a place where bone

destruction temporarily ceased and bone repair began. The increased bone destruction and bone repair seen in Paget's disease are closely similar to those seen throughout the skeleton in the osteitis fibrosa generalisata of hyperparathyroidism. There is one important difference: in osteitis fibrosa generalisata, that bone is destroyed which can best be spared; in Paget's disease, bone is destroyed without regard to structure. If a bone containing Paget's disease is immobilized, as after a fracture, the lack of stress and strain, in all probability abetted by the alarm reaction of Selye, curbs the overactivity of the osteoblasts, and the serum phosphatase level, an index of bone formation, falls. The initial disturbance causing bone destruction persists. There results imbalance between bone destruction and bone formation. The increased calcium and phosphorus coming from the bone leads to hypercalciuria and hyperphosphaturia. The capacity of the kidney to excrete calcium may be overtaxed, with a resulting hypercalcemia; if fluids are not forced, if the diet is not kept low in calcium and if immobilization is not kept at a minimum, a so-called chemical death from hypercalcemia may supervene. The authors describe studies on 2 patients with Paget's disease who sustained fractures. The aforementioned chain of events up to and including the hypercalcemic stage took place in these cases.

231:377-404 (Sept. 14) 1944

Psychiatric Casualties of War and Their Treatment. W. Overholser.—p. 377.

*Potassium Bicarbonate: Adjunct to Chemotherapy in Pneumonia Complicating Cardiac Decompensation; Preliminary Report. J. Ohnysty and W. Q. Wolfson.—p. 381.

*Fulminating Meningococcemia: Demonstration of Intracellular and Extracellular Meningococci in Direct Smears of Blood. W. P. Boger.—p. 385.

Thoracic Surgery (concluded). J. W. Strieder.—p. 388.

Potassium Bicarbonate and Sulfonamides in Pneumonia.—Ohnysty and Wolfson utilized the diuretic effect of potassium and the alkalizing effect of its bicarbonate in treating patients with severe heart damage who were receiving sulfadiazine for pneumonia. They found that patients so treated drink somewhat more liquid than do those given sodium bicarbonate, but they excrete almost twice as much urine and eliminate over 250 cc. more of retained fluid each day. By promoting excretion of retained water and sodium, potassium facilitates the reestablishment of cardiac composition. The authors give potassium bicarbonate to all patients whose cardiovascular status is classified as grade 3 or 4 whenever they receive sulfonamides. Its use is being extended to milder cases as prophylaxis against decompensation. Ten Gm. is given with the initial dose of sulfonamide and 2.5 Gm. every four hours thereafter until twenty-four hours after discontinuance of chemotherapy. Although apparently of low toxicity, potassium bicarbonate is not used when severe renal impairment or adrenocortical insufficiency is suspected.

Fulminating Meningococcemia.—Boger observed meningococci by direct examination of the peripheral blood smear in a case of fulminating meningococcemia that may also have been a case of the Waterhouse-Friderichsen syndrome. A woman aged 27 had been perfectly well until eight hours before admission, when she appeared to have influenza. Four hours later, when a blood specimen was taken, several petechiae were noted on the forearm. The following morning the patient complained of severe pains in the muscles and joints and presented a generalized purpuric rash. A blood specimen was taken for culture and examination and at the same time 10 Gm. of sodium sulfadiazine was given intravenously. The temperature was 103 F., the pulse rate 110 and the respiratory rate 24. The white cell count revealed 99 per cent neutrophils. Some of the polymorphonuclear cells were found to contain phagocytized gram negative diplococci. Extracellular organisms were also observed. At noon the patient was given a 500 cc. transfusion. Antimeningococcus serum was not available. Four cc. of adrenal cortex extract was given intramuscularly. The purpuric spots enlarged and new petechiae appeared. That evening intracutaneous extravasations too large to be covered by the outspread hand were present over the thorax and the extremities, and extravasations of smaller size were present on the face. The patient could not be roused. She gradually went into a state of vasomotor collapse and died. Permission for necropsy was not granted, so that doubt remains whether there were adrenal hemorrhages. The diplococci seen in the blood smears were cultured from the blood stream and found to be meningococci. The Waterhouse-Friderichsen syndrome is an overwhelming septicemia that produces purpuric subcutaneous extravasations and bilateral adrenal hemorrhages. Although meningococcic infections usually produce this syndrome, overwhelming sepsis due to other organisms occasionally gives rise to similar adrenal hemorrhages. Not all patients who die with the clinical picture of the Waterhouse-Friderichsen syndrome present adrenal hemorrhages. Hence it seems ambiguous to use the term "recovery" in speaking of the Waterhouse-Friderichsen syndrome, since the adrenal hemorrhages can be inferred only if the patient recovers. Clinically the term "fulminating meningococcemia" seems preferable to "Waterhouse-Friderichsen syndrome," and the latter should be restricted to pathologic discussions.

New York State Journal of Medicine, New York

44:1839-1950 (Sept. 1) 1944

Treatment of Infection with Particular Reference to Peritoneum. S. C. Harvey.—p. 1883.

*Role of Penicillin in Treatment of Compound Fractures. G. K. Carpenter and K. F. Mech.—p. 1886.

*Prophylaxis and Therapeusis of Clostridial Infections (Gas Gangrene). A. H. Dowdy, R. L. Sewell and J. G. Vincent.—p. 1890.

History of Drinking Habit in 400 Inmates of Penal Institution, with Special Consideration of Personality and Prognosis. P. Wenger.—p. 1898.

Voice and Breathing Disabilities Following Thyroid Surgery. C. G. Heyd.—p. 1905.

Human Tooth Injuries. O. C. Hudson.—p. 1910.

Penicillin in Compound Fractures.—Carpenter and Mech state that the compound fracture is the major problem in the orthopedic casualties returned to this country. Efficient first aid, plasma, blood transfusions, the sulfonamides and the open wound treatment have served to minimize infection and mortality. Penicillin is a more effectual antibacterial agent than the sulfonamides in both the prevention and the cure of infection. It has likewise proved valuable in the prevention of reinfection following reconstructive operative procedures. This factor has made it possible to perform major surgery sooner after complete wound healing than had been the case with the use of the sulfonamides. Penicillin therapy must be recognized and accepted as an adjunct only in the management of a surgical problem. Penicillin cannot replace a well planned surgical program. Penicillin assumes the role of only an effective antibacterial agent in the treatment of compound fractures.

Clostridial Infections (Gas Gangrene).—Dowdy and his associates investigated gas gangrene in more than 1,400 dogs in which the disease was experimentally produced. A variety of agents have been tested, such as roentgen therapy, subcutaneous and intramuscular oxygen, sulfadiazine, sulfathiazole, sulfanilamide, penicillin and pentavalent antitoxin. The infectious agents were virulent cultures of Clostridium perfringens, Clostridium septicum, Clostridium novyi (two strains) and Clostridium sordelli, employed either singly or in combination. The combined clostridial inoculums, in addition, contained a strain of Staphylococcus aureus. Experimentally, sulfadiazine has proved to be extremely efficacious in its prophylactic use against Cl. perfringens, Cl. septicum and Cl. sordelli infections in dogs when the disease is produced by individual pure cultures and when produced by a mixed culture of these same organisms contaminated by Staph. aureus. None of the sulfonamides were found to be effective against the disease when produced by Cl. novyi. Therapeutically sulfadiazine is far less effective, but from their limited clinical use of this drug the authors feel that it has been of value. Experimentally, penicillin and pentavalent gas gangrene antitoxin are both powerful therapeutic agents. The latter is the more valuable of the two if used late in the disease, because of its toxin neutralizing effect. Antitoxin must be used in large amounts and the entire dose given within a relatively few hours. The possibility of an anaphylactoid reaction must be borne in mind. The patient should be tested for sensitivity and, if he is sensitive, desensitization should be carried

out. During the period of desensitization, sulfadiazine or penicillin should be used, preferably the latter. The authors found no contraindication to combined therapy with all three of the agents discussed. Rather, they have an additive effect.

Northwest Medicine, Seattle

43:219-241 (Aug.) 1944

Alarming Increase in Incidence of Foreign Bodies in Tracheobronchial Tree. B. L. Titus.—p. 222.
Thyroiditis. A. J. Bowles.—p. 225.
Oblique Fractures of Both Bones of Lower Leg. L. H. Edmunds.—p. 227.
Carbon Tetrachloride Poisoning. T. E. P. Gocher.—p. 228.
Facial Deformity and Change in Personality Following Corrective Surgery. C. M. MacKenzie.—p. 230.
Absence of Daily Rhythm of Growth of Malignant Neoplasms. W. B. Dublin.—p. 232.

43:243-270 (Sept.) 1944

Group Psychotherapy in Military Medicine. F. J. Hamilton.—p. 247.
Evaluation of Ectopic Pregnancy. W. J. Reich and H. E. Silverman. —p. 252.
Photoroentgen Surveys of Industrial Workers in Washington. L. M. Farner and E. H. Laws.—p. 255.
Sedimentation Rate as We See It in Laboratory. A. VanDell.—p. 256.
Impalement of Rectum: Case Report. L. R. Hutchins.—p. 258.
Swallowed Lead Bullet. T. W. Houk.—p. 259.
Medical Etymology. H. H. Kretzler.—p. 260.

Oklahoma State Medical Assn. Jour., Oklahoma City

37:339-384 (Aug.) 1944

Analysis of Modern Treatment of Severe Burns. C. K. Drinker. —p. 339.
Public Health Aspects of Infantile Paralysis. G. F. Mathews.—p. 346.
Significance of Abnormal Spinal Fluid Findings in the Diagnosis and Treatment of Neurosyphilis. W. E. Graham.—p. 349.

37:385-434 (Sept.) 1944

Modern Concepts in Treatment of Syphilis. C. B. Taylor.—p. 385.
Ruptured Intervertebral Disk. A. H. Ungerman.—p. 388.
Rheumatic Fever. C. H. Hall.—p. 391.
Some Laboratory Phases of Clinical Diagnosis. I. H. Nelson.—p. 394.

Public Health Reports, Washington, D. C.

59:1131-1162 (Sept. 1) 1944

*Influenza Epidemic of Winter of 1943-44 in United States: Preliminary Summary. Dorothy F. Holland and S. D. Collins.—p. 1131.

Influenza Epidemic in Winter of 1943-1944.—Holland and Collins report an outbreak of a mild type of influenza which started in Minnesota and the Great Lakes region about the middle of November 1943. From the North Central region the epidemic spread eastward to New England, the Middle Atlantic states, Kentucky, Virginia, West Virginia, Delaware and Maryland, outbreaks being reported subsequently in the Mountain and Pacific states, the Southeast (Central and Atlantic) and, finally, the West South Central states. The Army as well as the civilian population experienced the epidemic. The tendency of influenza to occur in pandemic form "in cycles with intervals of several decades" led to concern that the 1943 outbreak might assume the characteristics of the 1918 pandemic. This apprehension was increased by the fact that in November, when the first indications of an outbreak were observed in this country, influenza had already attained epidemic proportions in England and Wales. However, the sharp rise in influenza deaths in the 126 large cities of England and Wales in November and December was found to be due not to the virulence of the causative organism but to a high case incidence. The subsequent course of the outbreak in the United States as well as the experience of other countries gives no evidence of a recurrence of the severe type of influenza observed in the 1918 pandemic. Characteristic features of the disease were the sudden onset, moderate prostration, fever and general pains, followed by great weakness. The duration was between three and five days. The laboratory evidence indicates that the outbreak was probably largely due to influenza virus A. The death rate from all causes during an influenza epidemic is an especially significant measure of its severity, the excess mortality relative to that in a nonepidemic period representing deaths associated with the epidemic. They found that for a group of ninety large cities the mortality from all causes in excess of the normal expectancy during the eleven weeks from Nov. 21, 1943 to Feb. 5, 1944 amounted to 50 per hundred thousand of population. This figure may be compared with total excess rates from all causes for a group of thirty-five large cities of 65 per hundred thousand for the epidemic of 1928-1929, 48 for that of 1926, 50 for that of 1923, 34 for that of 1922, 125 for the epidemic of 1920 and 598 for the pandemic of 1918-1919. Thus the current outbreak was larger than any epidemic since 1928-1929 but caused only about 8 per cent as many excess deaths in the United States as the 1918 pandemic. An interesting feature of the epidemic in England and Wales was the action taken to relieve the acute shortage of civilian medical personnel. An arrangement was made for the deferment from induction into the services of some 300 junior house physicians. In addition, the Royal Army Medical Corps made available hundreds of army doctors to assist in the care of influenza cases among civilians, representing the first instance of such cooperation between military and civilian medical personnel.

Radiology, Syracuse, N. Y.

43:213-318 (Sept.) 1944

*Adenoma of Bronchus: Clinical and Roentgenologic Study, with Report of 7 Cases. T. Lowry and L. G. Rigler.—p. 213.
Iodinated Organic Compounds as Contrast Media for Radiographic Diagnosis: III. Experimental and Clinical Myelography with Ethyl Iodophenylundecylate (Pantopaque). T. B. Steinhausen, C. E. Dungan, J. B. Furst, J. T. Plati, S. W. Smith, A. P. Darling and E. C. Wolcott Jr., with S. L. Warren and W. H. Strain.—p. 230.
Id.: IV. Pantopaque Myelography. G. H. Ramsey, J. D. French and W. H. Strain.—p. 236.
Myelography with Pantopaque and New Technic for Its Removal. W. G. Scott and L. T. Furlow.—p. 241.
Radiation Therapy of Lymphoid Tissue in Nasopharynx and Pharynx. H. H. Ashbury.—p. 250.
Roentgen Treatment of Lymphoid Tissue in Nasopharynx. S. J. Hawley.—p. 254.
Quantitative Study of Effect of Temperature on Sensitivities of X-Ray Screens and Films. R. H. Morgan.—p. 256.
Roentgen Diagnosis of Hypertrophic Pyloric Stenosis in Infants. H. W. Hefke.—p. 267.
Castration for Advanced Malignant Growth: A Short Historical Review with Case Report. W. E. Howes.—p. 272.
Leukemia in Radiologists. H. C. March.—p. 275.
Leukemia in Mice Following Exposure to X-Rays. P. S. Henshaw. —p. 279.
Industrial Radiation Hazards. C. B. Braestrup.—p. 286.

Adenoma of Bronchus.—Bronchial adenoma is a true tumor and the associated bronchiectasis, rather than being the cause of the growth, results from the long-standing obstruction of a bronchus. The most generally held view is that bronchial adenomas arise from the duct epithelium of the bronchial mucous glands. The adenoma is a smooth, round or oval, pinkish tumor. The intrabronchial growth is frequently polypoid and may be pedunculated. In some instances, however, it is flat, sessile and attached by a broad base. There is often extension through the bronchial wall, with formation of an extrabronchial mass which may be larger than the intrabronchial portion. Although adenoma of the bronchus almost always remains benign as far as lethal metastasis is concerned, its effects on the lung are extremely serious and in many instances ultimately cause death. The tumor grows slowly and gradually occludes the bronchus. During this process repeated infections occur distal to the obstruction, and sooner or later the portion of lung involved is destroyed by recurring suppuration. Bronchiectasis is regularly produced, and more acute infectious processes such as suppurative pneumonia, pulmonary abscess and empyema may occur and eventually prove fatal. A diagnosis of bronchial adenoma is usually easily established by roentgenologic and bronchoscopic examination, once the condition is suspected. The chief reason for differentiating between bronchial adenoma and bronchiogenic cancer is that adenoma of the bronchus has a prognosis quite different from that of cancer and therefore permits the employment of a more conservative plan of therapy in properly selected cases when radical resection would be attended by a great risk. Seven cases are presented to illustrate (*a*) the typical clinical features of intrabronchial adenoma, (*b*) bronchial adenoma with an extrabronchial mass, (*c*) the various types of roentgen examination used in the diagnosis, (*d*) the value of body section roentgenography in the delineation of the tumor and in following the effects of treatment and (*e*) the results of various types of therapy in the several cases, namely no treatment, local extirpation and pulmonary resection.

Surgery, Gynecology and Obstetrics, Chicago

79:225-336 (Sept.) 1944

*Fractures of Carpal Scaphoid in Canadian Army: Review and Commentary. J. C. Dickison and J. G. Shannon.—p. 225.
Calcium Changes in Acute Pancreatic Necrosis. H. A. Edmondson and C. J. Berne.—p. 240.
Experimental Studies in Peripheral Nerve Surgery: I. Effect of Sulfonamide Drugs on Experimental Gunshot Wounds Involving Peripheral Nerves. L. Davis, G. Perret and W. Carroll.—p. 245.
Id.: II. Effect of Sulfonamide Drugs on Regeneration of Peripheral Nerves. L. Davis, F. Hiller, G. Perret and W. Carroll.—p. 250.
Perilunar Dislocation of Carpal Bones and Dislocation of Lunate Bone. W. R. MacAusland.—p. 256.
Injuries of Vertex of Skull, with Special Reference to Paracentral Lobules of Brain. J. R. Green and E. Odberg.—p. 267.
Vaginal Hysterectomy: Evaluation of Gellhorn-Emmert Modification of Dickinson Technic in 600 Cases. F. V. Emmert.—p. 277.
Surgical Experiences with Abdominal Wounds in North African Campaign. E. L. Rohlf and J. M. Snyder.—p. 286.
*Vagotomy in Therapy of Peptic Ulcer. V. A. Weinstein, R. Colp, F. Hollander and E. E. Jemerin.—p. 297.
*Surgical Treatment of Corrosive Gastritis. K. A. Meyer and F. Steigmann.—p. 306.
Hook Traction Under Zygomatic Arch in Cervical Spine Injuries. W. T. Peyton, H. B. Hall and L. A. French.—p. 311.
*Posterior Mediastinal Goiter. J. M. Mora, H. J. Isaacs, S. H. Spencer and L. Edidin.—p. 314.
Cosmetic Method of Operating on Varicose Veins. B. Hejduk.—p. 318.
Sulfonamides as Adjunct to Treatment of Compound Fractures. G. V. Foster.—p. 323.
Clinical and Laboratory Evaluation of Action of Sulfonamide Ointments. J. R. Cochran.—p. 326.

Fractures of Carpal Scaphoid.—Dickison and Shannon present the results of a study of 257 cases of fractured carpal scaphoids occurring in approximately three years in the Canadian army overseas. The most common fracture is a transverse one through the body of the bone, usually occurring at the waist or the center of the body. The statistical analysis of the 257 cases shows that 196 involved the waist of the scaphoid, 38 involved the proximal pole and 23 involved the tubercle. The most important problem of fracture of the scaphoid is early diagnosis. The authors analyze the results of treatment with regard to the time of diagnosis. Fractured scaphoid diagnosed early and properly treated will almost invariably unite. By proper treatment is meant reduction of displacement, if present, and uninterrupted immobilization with the wrist in extension and radial deviation until union occurs. It is probably true that a fractured scaphoid never unites if left untreated. Will such fracture if left untreated invariably lead to a painful wrist in later life? Some patients carry on for long periods with only a minimum of discomfort. Some are symptom free for a long period, and when injured a second time their symptoms are relieved by a short period of immobilization. That some of them develop disability in later life is undoubtedly true. How to obtain union consistently in these late diagnosed fractures within a reasonable time is still an unsolved problem. Immobilization was often unsuccessful in the cases presented in this report. The criticism might be made that the immobilization was not carried on long enough. There is danger of persisting in this form of treatment too long without evidence of progress toward union. Complete or partial excision is of no use in these fractures. Union may be obtained by a grafting operation, but this is difficult. The late fracture with degenerative arthritis is an arthritis problem and must be treated as such. Union of the fracture will not relieve the symptoms, and palliative treatment is all that can be offered, fusion of the wrist being the last resort and warranted only by severe disability. The patient with a fractured scaphoid may be able to carry on his occupation during the long period of treatment. Often, however, this is impossible and there is serious economic loss.

Vagotomy in Peptic Ulcer.—Weinstein and his collaborators report 6 clinical cases in which vagotomy was performed either alone or in conjunction with some other operative procedure. Most of these cases had not responded to ordinary measures. In 3 cases the lesion was a gastrojejunal ulcer following partial gastrectomy, in 2 it was a duodenal ulcer, and in 1 there existed severe functional complaints without demonstrable organic lesion. In only 2 cases was complete vagotomy attempted, but in neither of these was it achieved. The validity of the insulin test as an index of persistent vagal innervation was upheld by the studies in these cases. In none of the cases was evidence of beneficial therapeutic effect obtained. Gastric vagotomy alone cannot be recommended as a therapeutic procedure.

Corrosive Gastritis.—Meyer and Steigmann state that the surgeon usually sees these patients when they begin to suffer from the sequelae of corrosive gastritis. These sequelae are manifested by symptoms of pyloric obstruction. Since they may not be evident until many months following the intake of a corrosive substance, the patients often do not associate their present symptoms with the past mishap. Therefore the patient should be asked directly as to a possible intake of a corrosive substance. The history is of great importance in corrosive gastritis, because except for the history of ingestion of a corrosive substance there is rarely any other way by which it can be diagnosed before operation. In many instances the diagnosis may not be made by the surgeon even at operation if he is not aware of such a condition. It is important to differentiate between corrosive gastritis and carcinoma not only from the point of view of prognosis but also from the point of view of treatment, as corrosive gastritis requires different preparation and operation. In many cases of corrosive gastritis two stage operations may be necessary, i. e. primary jejunostomy and secondary gastroenterostomy at a later date, while in carcinoma this is rarely advisable. The patient with corrosive gastritis does not present an emergency case and all possible measures should be taken to build him up before surgery is undertaken. Gastroenterostomy rather than resection may be done, as the dangers of secondary gastrojejunostomy ulceration are minimal since there is no free acidity. Patients with corrosive gastritis have to be prepared carefully and for a long time, if necessary, by jejunostomy feedings, for the final operation on the stomach. In some cases with very small fundic pouches "sham feedings" have to be given in order to distend this portion sufficiently to permit the gastroenterostomy. The authors present representative histories of 4 patients with corrosive gastritis seen at the Cook County Hospital.

Posterior Mediastinal Goiter.—Partially intrathoracic goiters occur relatively often. Completely intrathoracic goiters are much rarer. The rarest of the intrathoracic goiters is the type found in the posterior mediastinum. Only 6 such cases have been previously recorded. The case here reported by Mora and his associates is the seventh to be recorded. A woman aged 55 was admitted to the hospital in November 1942 complaining of increasing weakness, nervousness, palpitation and weight loss. She had not been feeling well for about eight years, having noted increasing fatigue on slight exertion, profuse perspiration, heat intolerance and tremor of the fingers. From time to time she would have bouts of nervousness, weakness, irritability and palpitation. She had been studied by several doctors, all of whom found on x-ray examination of the chest a large shadow occupying the right upper lung field. She was advised to do nothing about this mass. Examination by the authors disclosed tremor of the fingers, basal metabolic readings between +45 and +51 and a large globular mass occupying the right upper thoracic cavity; on lateral views this mass was seen to lie in the posterior mediastinum. The diagnosis at this time was thyrotoxicosis, and the mass was believed to be a large intrathoracic goiter. At operation the neck was opened through the usual collar incision and the strap muscles were separated. Preliminary exploration revealed no thyroid tissue in the neck. On further dissection a small cystic lobe was found on the left, just at the superior thoracic aperture. This was easily removed. On the right, a thin attenuated pole was found just below the level of the first rib; this was secured and divided between ligatures. On further exploration a large mass was encountered posteriorly, lying entirely within the thoracic cage. On careful finger dissection, hugging the margins of the mass and with gentle traction upward, the tumor was gradually freed. A hemostat was then plunged into the mass, and the liquid and jelly-like contents were removed by suction. This procedure permitted narrowing of the transverse diameters of the thoracic goiter, following which it was easy to deliver the entire mass. The patient was discharged in good condition on the tenth postoperative day. One year after operation the basal metabolic rate was +6.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Ophthalmology, London

28:429-480 (Sept.) 1944

Contribution to Study of Anophthalmia, with Description of Case. T. Rogalski.—p. 429.
*Study of 84 Cases of Delayed Mustard Gas Keratitis Fitted with Contact Lenses. Ida Mann.—p. 441.
Note on Rosettes, Nature and Nomenclature of "Glioma Retinae." E. Wolff.—p. 448.
Virus Ophthalmia Neonatorum. A. Sorsby, Elizabeth E. Hoffa and Elizabeth N. Young.—p. 451.
Incomplete Avulsion of Eye: Report of Case. I. C. Michaelson. —p. 458.
Gas Mask Wafer for Presbyopia. W. O. G. Taylor.—p. 461.

Delayed Mustard Gas Keratitis.—Since 1937, when the condition of delayed mustard gas keratitis was first beginning to be recognized, Mann has examined a relatively large number of cases; 84 have passed through the contact lens clinic at Moorfields. All the patients gave a history of exposure to mustard gas in 1917 or 1918. The diagnosis was made on the history and on the finding of the typical mustard gas scars with corneal degeneration, varicose conjunctival and corneal vessels and avascular scars on the interpalpebral conjunctiva. The patient does not generally connect the delayed keratitis with the exposure to gas. Most of them did not notice anything until the ulceration stage began. Only 8 of the patients stated that the sight of one or both eyes had never been so good as before the gassing and that they had had some sort of eye trouble ever since. The recurring ulcers heal but tend to leave faceted scars, which gradually diminish visual acuity. Repeated attacks and a slowly deteriorating visual acuity, relieved by wearing contact lenses, is typical of roughly 46 per cent of the cases. What their subsequent fate will be is not yet known. That wearing contact lenses does not entirely prevent breakdown and further deterioration of sight seems certain, but it is equally certain that in a number of cases retention of visual acuity and continuance in work has been made possible for many years. Patients with mustard gas lesions usually have very good tolerance for contact lenses, both on account of the relative insensitivity of their corneas and on account of the vast improvement in visual acuity, which acts as a spur to success. Thirty-nine of the 84 patients wear the lenses with comfort during the working day. Of these 39 patients 20 have had relapses since wearing the lenses. Thirteen of these have had far fewer relapses than before wearing the lenses. Small shallow ulcers heal fairly quickly with mild mydriatics and heat. Deeper ulcers, discharging cholesterol and fatty débris from the base, take longer to heal and may require tarsorrhaphy. Superficial plaques, raised from the surface, of degenerative material may mechanically interfere with the wearing of a contact lens and should be scraped off.

British Journal of Urology, London

16:35-80 (June) 1944

Diagnosis and Treatment of Infections of Male Genital Organs Other Than Tuberculosis and Gonorrhea. J. C. Ainsworth-Davis.—p. 35.
Notes on Topography of Congenital Kidney Malformations. T. Zondek. —p. 41.

British Medical Journal, London

2:233-262 (Aug. 19) 1944

*Scurvy: Survey of 53 Cases. R. B. McMillan and J. C. Inglis. —p. 233.
Urticarial Reactions and Desensitization in Allergic Recipients After Serum Transfusions. Kate Maunsell.—p. 236.
*Incidence of Bleeding Gums Among R. A. F. Personnel and the Value of Ascorbic Acid in Treatment. W. P. Stamm, T. F. Macrae and S. Yudkin.—p. 239.
Incidence of Gingivitis in Royal Air Force. G. A. Smart.—p. 242.
Rupture of Aortic Aneurysm into Duodenum. J. E. Morison.—p. 244.

Scurvy.—McMillan and Inglis review observations on 53 patients with scurvy. There were 48 men and 5 women. The patients ranged in age from 41 to 82 years; 43 were over 65. The disease observed was typical "bachelor" scurvy. There were three root causes. First and most important was ignorance, mainly in men, of the need for potatoes and vegetables in the diet. Second was apathy leading to neglect of the same items because they required preparation and cooking. Third was poverty, making it impossible to buy an adequate diet or live anywhere but in the worst type of lodging with poor cooking facilities. The first factor was not so significant in peacetime, as many countered it by eating fruit. Wartime scarcity of fruit without a compensatory increase in the intake of potatoes and vegetables resulted in such persons developing scurvy. It is suggested that as long as the scarcity of fruit exists the concessions at present enjoyed by children and expectant mothers should be extended to the elderly. Clinically the only unusual complaint was lumbago, which probably was the result of small deep hemorrhages in the muscles of the back. Although in no patient was the blood picture completely normal, in some it was nearly so, and agreement is reached with the opinions of others that (*a*) anemia and scurvy need not coexist in man, (*b*) when they do coexist the anemia often bears no relation to the extent of the hemorrhages or the plasma ascorbic acid content and (*c*) the anemia is varied in morphologic type, being mainly normocytic. The authors suggest that the anemia of scurvy is due to a complex deficiency, with vitamin C acting only as an adjuvant.

Bleeding Gums and Ascorbic Acid.—Stamm and his associates investigated the incidence of bleeding gums in the Royal Air Force and aimed to assess the value of ascorbic acid in the treatment of this condition. All personnel available were examined, except those already taking ascorbic acid, those being treated for acute ulcerative gingivostomatitis and those with no teeth. All those included in this experiment had been living on service rations for six months or more. The gums of the lower jaw were examined for bleeding after digital massage. Alternate members of the group with bleeding gums were given ascorbic acid tablets and dummy tablets flavored with tartaric acid. The dose of ascorbic acid was 200 mg. daily for seven days, followed by 100 mg. daily for fourteen days; the dummy tablets were similar in appearance and taste and were given in similar numbers. At the end of the experimental period all subjects given ascorbic acid and dummy tablets were reexamined. The original notes were not available to the examiner, so that he could not be influenced by his previous observations or by a knowledge of which tablets had been given. The ascorbic acid content of the food served to the airmen in the messes was determined by the dichlorophenol-indophenol technic. The average amount of ascorbic acid present in the food served to airmen was 25.8 mg. per man daily during October and November 1941 and 16.8 mg. during March 1942. On examination of 2,962 personnel, 588 (19.8 per cent) were found to have some degree of bleeding of the gums, a similar incidence being found in the autumn and spring and at each of the stations. No greater improvement in the gum conditions was obtained by treatment with ascorbic acid than with control tablets. Observation of 600 personnel over a six weeks period showed that there was a large normal variation in the degree of bleeding of the gums, irrespective of treatment. Those having "sponginess" as well as bleeding of the gums showed no greater improvement with ascorbic acid treatment than with dummy tablets. Patients' personal opinions as to the efficacy of treatment bore no relation to the objective signs.

2:263-296 (Aug. 26) 1944

Psychologic Medicine and the Family Doctor. R. D. Gillespie.—p. 263.
*Episode of "Homologous Serum Jaundice." W. H. Bradley, J. F. Loutit and Kate Maunsell.—p. 268.
Late Results of Closed Intrapleural Pneumolysis. P. W. Edwards, A. C. Penman and J. Logan.—p. 270.
High Tone Deafness in School Children Simulating Mental Defect. Mary D. Sheridan.—p. 272.
"Explosive" Outbreak of Hemolytic Streptococcal Tonsillitis on an R. A. F. Station. T. S. Wilson.—p. 275.
Treatment of Rheumatoid Arthritis with Bismuth. A. H. Douthwaite. —p. 276.

Homologous Serum Jaundice.—According to Bradley and his associates the occurrence of jaundice in man after the administration of human blood products is now a well recognized phenomenon. The jaundice, which is of hepatic origin, is readily distinguished from the hemolytic icterus which may arise immediately after transfusion with incompatible blood or out of date stored blood. Clinically it is similar to, if not

indistinguishable from, epidemic hepatitis (catarrhal jaundice), but the incubation period is unusually long—commonly from two to three months, in contradistinction to the twenty to forty day period in epidemic hepatitis. A high incidence of this jaundice has been observed among 71 subjects during the course of an investigation into allergic reactions to human serum. All these subjects received pooled human serum from a single batch (No. 034). Subsequently icterogenicity was confirmed by the results of the deliberate administration of this batch to 4 volunteer patients with rheumatoid arthritis in whom it was desired to produce jaundice for therapeutic reasons. Forty-seven subjects received intradermal skin tests with batch 034. Nine subjects received intradermal skin tests and serum transfusions with batch 034. Nineteen received skin tests or transfusions or both with batch 034 and, in addition, tests or transfusions with other human material. Of these, 7 were allergic subjects, 8 were nonallergic controls and 4 were the patients with rheumatoid arthritis. All except 2 subjects were followed up for at least one hundred and fifty days after exposure. Of the 47 patients who had received batch 034 only as skin tests, 26 developed jaundice. Similarly, of the 9 who had batch 034 only as skin tests and transfusions, 5 developed jaundice. Of the 19 patients who received other materials as well as batch 034, 11 developed jaundice. The authors point out that the cases of jaundice in the present series had been regarded as "catarrhal jaundice" and the association with the administration of blood products was at first not recognized. The diagnosis of homologous serum jaundice was established only by the follow-up. Jaundice occurred in 57 per cent of the persons exposed. The dose of homologous serum administered varied from 0.1 to 1,200 cc. The severity of the disease was not related to the dosage of serum given or to the route of administration.

Journal of Endocrinology, London

4:1-102 (July) 1944

Artificial Induction of Lactation in Bovine by Subcutaneous Implantation of Synthetic Estrogen Tablets. S. J. Folley and F. H. Malpress.—p. 1.
Fracture of Pelvic Bones in Bovines Implanted with Tablets of Synthetic Estrogens. A. T. Cowie.—p. 19.
Artificial Induction of Lactation in Bovines by Oral Administration of Synthetic Estrogens. S. J. Folley and F. H. Malpress.—p. 23.
Chemical Composition of Bovine Mammary Secretions Induced by Subcutaneous Implantation or Oral Administration of Synthetic Estrogens. S. J. Folley and F. H. Malpress.—p. 37.
Experiments on Use of Tablets Containing 50 per Cent Hexestrol for Artificial Induction of Lactation in Bovine. S. J. Folley, D. L. Stewart and F. G. Young.—p. 43.
Estrogen Treatment of Cattle: Induced Lactation and Other Effects. J. Hammond Jr. and F. T. Day.—p. 53.
Estrogen Excretion in Milk from Estrogenized Cattle. W. Lawson, S. W. Stroud and P. C. Williams.—p. 83.
Induction of Lactation in Heifers by Single Injection of Esters of Diethylstilbestrol. A. S. Parkes and R. E. Glover.—p. 90.

Lancet, London

2:231-264 (Aug. 19) 1944

Year of Military Medicine in India. A. W. D. Leishman and A. R. Kelsall.—p. 231.
Wounds of Joints. H. Fruchaud.—p. 235.
*Acridines in Septic Wounds: Use of 5-Aminoacridine. H. R. G. Poate.—p. 238.
Talocalcanean Articulation. F. W. Jones.—p. 241.
Air Embolism in Criminal Abortion. D. Teare.—p. 242.
Estimation of Thiouracil in Urine. A. B. Anderson.—p. 242.
Orthopedic Anesthetist. B. G. B. Lucas and I. A. G. L. Dick.—p. 243.
Primary Tuberculous Infection in Nurses: Manifestations and Prognosis. M. Daniels.—p. 244.

Acridines in Septic Wounds.—According to Poate 5-aminoacridine is stainless, is stable in solution, has a p_H of 6 and is innocuous to human tissues in 1:1,000 solution. In an Australian general hospital 5-aminoacridine was chiefly used, but 2:7-diaminoacridine was also tested. The latter was not favored in the wards because of its staining propensity. Both these acridines were applied as powders (alone or with sulfanilamide) and in solutions of varying strength, but finally 1:1,000 became the standard concentration. When there was a pyocyaneus infection 2 per cent acetic acid was added. To get the best results all sequestrums and sloughs must be removed, drainage of deep wounds must be efficient, immobilization of fractures must be adequate and the patient's hemoglobin must be kept as near normal as possible. Closed plaster treatment was abandoned. The effect of the two acridines was that the wounds soon became surgically clean; healthy granulations promoted rapid healing. All purulent discharge ceased within a few days, thus relieving the patient of a continuous drain on his tissue proteins. As a result, transfusions were no longer necessary, appetite returned and patients put on weight. In no case treated by these two acridines was there a gravitational abscess, secondary hemorrhage or cellulitis. The authors review clinical experiences with 5-aminoacridine and 2:7-diaminoacridine in 120 cases, including 24 suppurating gunshot wounds of bone. The results have been very good. In all but 5 cases sepsis was immediately controlled. For general use in wards 5-aminoacridine is preferred because it does not stain fabrics and tissues. Where there is gross established sepsis, the wound may be irrigated with an aqueous solution of 5-aminoacridine (1:1,000) through Carrel tubes. For other purposes an emulsion may be made, or acridine in powder form may be mixed with sulfanilamide (1:10 to 1:40). Recent wounds associated with compound fractures have been treated with this powder after débridement and then closed by primary suture. 5-aminoacridine seems to be particularly effective against hemolytic staphylococci and appears to favor bone repair.

Arch. Urug. de Med., Cir. y Especialid., Montevideo

24:305-420 (April) 1944. **Partial Index**

Roentgen Study of Intestinal Tuberculosis. A. Rodríguez.—p. 305.
Extirpation of Cancer of Thoracic Esophagus. V. Armand Ugón, J. M. A. Leguisamo and R. Armand Ugón.—p. 363.
*Rh Factor. D. Invernizzi.—p. 396.

Rh Factor.—Invernizzi states that the percentage of positive distribution of the Rh factor is greater in mestizo people, Indians and colored people than in white people. The proportion is from 93 to 99 per cent in the former and 85 per cent in the latter. The presence of the Rh factor in the erythrocytes is determined by the reaction of 0.01 cc. of a 2 per cent solution of erythrocytes in isotonic solution of sodium chloride containing 0.02 cc. of anti-Rh serum, after contact of both constituents in a test tube for one hour in the water bath at a temperature of 37 C. Fresh blood is used because of the fact that the Rh factor is easily destroyed in the erythrocytes. A positive macroscopic reaction is shown by rugosities in the border of the globular sediment in the test tube. Moderate positive reaction with moderate agglutination is observed microscopically. Specimens of well known positive Rh and negative Rh blood are used as control tests. Repeated transfusion of blood from Rh positive donors to Rh negative individuals may provoke anti-Rh agglutinins in the blood of the latter. A test is performed after repeated transfusions for ascertaining the presence of isoimmunization or lack of it before further transfusion. The danger of post-transfusional reactions is acute in pregnant women who may have developed a condition of isoimmunization through the presence of the Rh factor in the blood of the fetus. The hydropic, acute icteric and congenital anemic forms of erythroblastosis fetalis are due to the presence of the Rh factor in the infant's blood. The condition may be found in one of two twins and not in the other in cases of heterozygotic transmission of the Rh factor by the father. The author advises use of negative Rh blood for transfusion to infants with any type of erythroblastosis fetalis, as well as to mothers of erythroblastosic infants and when repeated blood transfusions are given. Plasma should be used in emergencies.

Revista Clínica Española, Madrid

12:363-444 (March 30) 1944. **Partial Index**

*Pernicious Anemia and Hepatic Cirrhosis. M. R. Castex, E. S. Mazzei and J. Remolar.—p. 378.
New Aspects in Therapy of True Anthrax. M. Gómez Fresno.—p. 426.

Pernicious Anemia and Hepatic Cirrhosis.—Castex and his collaborators describe two types of macrocytic hyperchromic anemia complicating liver cirrhosis. One type is that of pernicious-like anemia. It is a frequent complication of liver cirrhosis and disappears on liver therapy. The second type is a true pernicious megaloblastic anemia of the Biermer-Addison type. It is a rare complication of liver cirrhosis and does not respond to liver therapy. It has an acute course and fatal prognosis.

Book Notices

X-Ray Examination of the Stomach: A Description of the Roentgenologic Anatomy, Physiology, and Pathology of the Esophagus, Stomach, and Duodenum. By Frederic E. Templeton, M.D., Head of the Department of Roentgenology, the Cleveland Clinic. Cloth. Price, $10. Pp. 516, with 297 illustrations. Chicago: University of Chicago Press: London: Cambridge University Press, 1944.

The time devoted to the x-ray examination in diseases of the digestive tract often seems to be in inverse ratio to the importance of the procedure. In this admirable book the technic of a detailed, painstaking search for abnormalities of the esophagus, stomach and duodenum, done with full consideration for the serious consequences which may result from the interpretation of the findings, is portrayed. This is a monograph representing essentially the experience of the author and his colleagues at the University of Chicago, but there are numerous quotations from the literature, and the bibliography is extensive. The most valuable portion of the book is the detailed description of the methods of x-ray examination of the upper digestive tract, with particular attention to the "filming fluoroscope." The technic of fluoroscopy is well described and illustrated by means of films exposed under fluoroscopic guidance. The descriptions of the normal variations of these structures and most especially of the physiology and pathology of the esophagus are especially instructive. The grouping together of the abnormalities of the esophagus, stomach and duodenum under such headings as inflammations, ulcer and neoplasm rather than treating each individually is somewhat forced, as the x-ray manifestations of the pathologic conditions of these organs are not especially similar. Likewise the placement of the section on differential diagnosis at the end of the book far removed from the original descriptions makes for some repetition. The illustrations are abundant, well chosen and well reproduced. Few exceptions can be taken to the author's conclusions. The designation of the term "phytobezoar" rather than "trichobezoar" for a hair ball is obviously an oversight. The contributions of Lewis Gregory Cole to the x-ray examination of the digestive tract are insufficiently stressed. The book suffers from the author's lack of sufficient experience or reluctance to offer an opinion when he has not had personal contact with a method or a problem. These criticisms are minor. The book as a whole is one of the finest contributions to roentgenologic diagnosis in the past decade and should be read assiduously by every physician who has interest in the diseases of the upper digestive tract.

Conference on Tuberculosis Isolation Sponsored by the California State Department of Public Health Held at Los Angeles March 20, 1943. [Editor: Edward Kupka, M.D.] Paper. Various pagination. Los Angeles, [n. d.].

This mimeographed, paper bound release is a virtually complete summary of the conclusions of the Conference on Tuberculosis Isolation sponsored by the California State Department of Public Health at Los Angeles on March 20, 1943. It is an effort to mobilize public opinion in support of the legal requirement not common in many states providing for enforced isolation of tuberculous patients with open lesions who fail or refuse to heed their responsibilities for preventing the spread of infection. Experience in Los Angeles County and the opinions of health officers, judges, sanatorium personnel and representatives of the state attorney general's office are set forth at length. This report should be valuable to tuberculosis control officers and, to a lesser extent, should be of interest to the voluntary tuberculosis associations.

First Hospitals in Tulsa. By Fred S. Clinton, M.D., F.A.C.S. Reprinted from The Chronicles of Oklahoma, Vol. XXII, Number 1, 1944. Paper. Pp. 28, with illustrations. Oklahoma City, 1944.

The author has preserved for the Chronicles of Oklahoma the story of the first hospitals in Tulsa, beginning in 1900, when the city had a population of only 1,390. It is principally a story of three hospitals in whose establishment and development the author had an active and directing part. The first was organized in 1900, a six room isolation cottage necessitated by the occurrence of a smallpox epidemic. Six years later the Tulsa Hospital Association was formed and a general hospital established, which also brought to this community the first training school for student nurses. The third hospital included in this historical account, the Oklahoma Hospital, was chartered Dec. 11, 1915. Other early hospitals are also mentioned with the hope that other writers of local history will at some future time furnish an extended account of the contributions and services of these institutions.

In writing this article the author has drawn from his own experiences and records and has also introduced documentary evidence of many of the events of this early hospital period. His work is of interest not only from a historical point of view but as a record of hospital problems and needs that occur in a new and growing community.

Dust Hazards in Australian Foundries. By A. A. Ross, B.Agr.Sc., and N. H. Shaw, B.Agr.Sc. Technical Report No. 1, Industrial Welfare Division, Department of Labour and National Service, Commonwealth of Australia. Paper. Pp. 45. Melbourne, 1943.

This pamphlet gives the results of a study of the dust hazards in the various processes in Australian foundries, sets up standards of permissible dust limits as determined by the Owens jet dust counter and makes recommendations for control in those operations found to have an unsafe concentration of dust. The review of the literature is merely that supporting the occurrence of pathologic changes in the lungs from exposure to industrial dusts. The authors discuss the recognized limitations of the Owens jet dust counter as compared to the Greenburg-Smith impinger. They apparently reached the conclusion that the practicality of the former outweighed whatever inaccuracies it may have after studying atmospheric conditions with both around the various foundry processes. They state that there was no definite correlation in the findings of the two; however, they do give standards of dust concentration as determined by the Owen jet dust counter which they feel are within safe limits for exposure of the workmen. They arrived at the inevitable conclusion that environmental conditions in Australian foundries as pertaining to dust should be improved.

Twenty-Second Hospital Yearbook. 1944 Hospital Purchasing File. Directory of Hospital Products, Manufacturers' Catalogs, Editorial Reference Section. Twenty-second edition. Boards. Price, $2.50. Pp. 912. Chicago: Modern Hospital Publishing Co., Inc., 1944.

This is an excellent reference book on hospital buying. It has an extensive directory of hospital products covering 360 pages with supplementary catalogues on clinical and scientific apparatus, general furnishings, food service equipment, laundry facilities and supplies, construction materials and plant equipment. An editorial reference section contains comprehensive check lists and other valuable information essential in the planning of hospital departments and services. The administrative officers and departments of hospitals will find this book a valuable and convenient source of reference. Its usefulness is further enhanced by a complete index of catalogues and advertisements, an alphabetical list of manufacturers and distributors and lists of hospital associations and national agencies serving the hospital and allied fields.

Handbook of Nursing in Industry. By M. Gray Macdonald, R.N. Cloth. Price, $2.50. Pp. 226. Philadelphia & London: W. B. Saunders Company, 1944.

This is a textbook of moderate detail dealing with the various functions of the nurse in industry. The descriptions and discussions in the twenty-six chapters include those phases which should be included in a well rounded program. Special attention is called to the modifications of a program in a bank, department store, restaurant and a mill village. The philosophy and practical experience of the author add materially to the stature of the book. It should find wide use in the added emphasis that is being given to industrial health education for nurses, both graduate and undergraduate.

Red Lights on the Horizon. By H. Ameroy Hartwell. Boards. Price, $1. Pp. 22. Illustration by Gladys Richcreek. Boston: Bruce Humphries, Inc., 1944.

Here is a new poem by Dr. Hartwell calling attention to the early signs and symptoms of disease. Whether or not this is the best technic to cause patients to see their physicians for early diagnosis is a matter of considerable doubt. Nevertheless the author must have had a good deal of pleasure in writing the poem.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

DEFECTIVE SPEECH AND POSSIBLE LEFT HANDEDNESS

To the Editor:—A 5 year old girl who appears to be normal in every other respect has a tendency toward left handedness and defective articulation. The flow of speech is smooth, but she substitutes y for l, d for sch or g and w for r. Thus "Mary had a little lamb" becomes, in her rendition, "Mawy had a yitta yamb," "the red school bus" becomes "the wed dool bus," and a "green" chair becomes a "deen" one. I once heard a professor of physiology who was afflicted with stammering attribute his difficulty to his being left handed but compelled to use his right hand, thus interfering with the speech center of Broca. When the child under consideration is eating, she is seen to carry the fork sometimes in her left hand, sometimes in her right. Because of the observed tendency for her to use her left hand, would it be advisable, as a preliminary to attempting to correct her defective articulation, to encourage her to use her left hand as the dominant one? Any other suggestions as to methods of correcting her speech will be appreciated. M.D., Alaska.

ANSWER.—It is not unusual for children of 5 to demonstrate this type of defect. Some children, although normal in other respects, are slow in learning the language skills—perhaps because of a slower maturation of the language centers of the cerebrum. They will often, as the child in question apparently does, substitute simpler speech sounds for the more complex, or sounds made at the front of the mouth for sounds made farther back. (Sight plays an important role in the acquisition of speech, and the child usually learns first the sounds whose essential movements can be easily seen and imitated, for example p, b, m, w. Conversely, he learns last the sounds whose essential movements are made farther back in the mouth and cannot be easily seen, such as r, k, g, ng.)

The tendency to ambidexterity may or may not be significant. It would be best to make no attempt to establish the dominance of one hand. Given time, the child will no doubt do this herself. In regard to correcting the speech defect, a daily period of speech drill is recommended. The defective sounds should be isolated and pronounced alone until the child can produce them correctly; later they can be incorporated into simple sound combinations and eventually into familiar words and phrases.

THYROID OR PITUITARY DEFICIENCY

To the Editor:—A girl of 18 is overweight and losing her menses, there is almost no flow, and occasionally she skips a month. The basal metabolic rate is — 23. If this case is one of pituitary origin is there any treatment and cure? She will receive some thyroid medication. Is it true that in a pituitary case cancerous changes always develop later in the abdomen or pelvis? M.D., New Jersey.

ANSWER.—It is difficult to decide whether irregular and scanty menstruation, obesity and a low basal metabolism are due to thyroid deficiency or pituitary disorder without having other information. Usually the determination of serum cholesterol would be helpful, since in thyroid deficiency not under thyroid treatment the cholesterol will be well above normal levels but in pituitary deficiency cholesterol is below the normal upper limits. It may be wise to try thyroid cautiously with basal metabolism check, to use a carefully limited diet to control the weight; and gonadotropic pituitary or pregnant mare's serum concentrate may be tried subsequently if this does not show a distinct tendency to correction of the difficulty.

There is no known reason to suspect that pelvic or abdominal malignant disease would follow in case this is a pituitary deficiency.

FOUL TASTE IN MOUTH DURING PREGNANCY

To the Editor:—Two years ago I rendered obstetric care to a patient who developed an intense foul taste in the throat in the third month of gestation, and this persisted until a day after delivery. Careful investigation of the sinuses, nose, mouth and throat proved negative. The patient is again pregnant and after six weeks' gestation has this same intense foul taste. Medication has not alleviated it. I would appreciate an opinion. M.D., New York.

ANSWER.—The search for an organic cause of the poor taste in the mouth should include a careful examination of the teeth. Decay in a tooth is often the focus of a bad taste. If no cause is found, a mouth wash of dilute hydrogen peroxide or 5 per cent potassium chlorate may help to control the discomfort. In rare instances the cause may be psychic in origin and little can be done toward its therapy.

OSTEOCHONDROSIS OF NAVICULAR (KÖHLER'S)

To the Editor:—A girl aged 2 years, in good health, began to stumble, fall and walk unsteadily, with a limp in the left leg. Complete investigation revealed no abnormalities excepting x-ray finding of irregularity and condensation of the left navicular consistent with the diagnosis of osteochondrosis, or Köhler's disease. Could you advise concerning current opinion as to etiology, therapy and prognosis? Jack H. Tabor, M.D., Dailey, W. Va.

ANSWER.—In the large majority of cases of Köhler's disease, or osteochondrosis, of the navicular bone, there is little pain or disability. A thorough search should be made to determine if there is any other existing condition which could account for the stumbling, unsteady walk and limp. The treatment of Köhler's disease is simple: surgery should not be done. About all that one can do is provide a little support in the shoe to hold up the longitudinal arch. Saddler's felt or piano felt pasted in the shoe is as good as anything.

TESTING FOR ALLERGY TO CATGUT

To the Editor:—I have come across several patients whom I have suspected of being sensitive to catgut. With the help of the allergy department I made up solutions of plain and chromic catgut in the following manner: I allowed a strand of each type of catgut to soak in absolute alcohol in the proportions of 10 to 1 for forty-eight hours. The allergist then made me several dilutions of 1: 100, 1: 10 and full strength, using Coca's solution as a diluent. I tested several patients with these solutions and obtained 2 plus reactions in several. However, on further control testing I found that the absolute alcohol itself causes a similar reaction. New solutions were then made up by soaking the catgut in Coca's solution for several days without the alcohol, and so far all my intradermal tests have been negative. Would you kindly tell me if an adequately potent extract of catgut can be obtained by the latter method of using just Coca's solution? M.D., North Carolina.

ANSWER.—Catgut is specially prepared tendinous tissue. This is not soluble in water or neutral saline solution. Allergy to catgut, therefore, is presumably due to the presence of minimal amounts of soluble proteins in improperly prepared catgut. To obtain a solution of this material, the catgut might be scraped with a razor blade or sharp edge of a broken piece of glass. The finer the shavings, the more likely soluble material may be obtained. The fine shavings may then be soaked in 0.2 per cent sodium carbonate for several hours or over night. A mechanical shaker or grinding in a mortar will help. After filtering, the solution should be neutralized with diluted hydrochloric or acetic acid to a p_H of about 7.0. It may be necessary to keep the material slightly alkaline, i. e. about 7.4, in order to avoid precipitation of the protein obtained by extraction. Therefore only a small portion of the solution should be neutralized at first to determine the p_H at which precipitation begins. The rest of the solution should be neutralized to a point where no precipitation will occur.

Phenol is then added as a preservative to a concentration of 0.5 per cent. After this the material is filtered through a Seitz or Berkefeld filter for sterility. The material must then be tried on a half dozen normal patients to make sure that it is not a primary irritant which will produce false positive reactions when 0.02 cc. is injected intradermally. If it proves to be irritating, it should be diluted with isotonic solution of sodium chloride to make a 1: 10 or 1: 100 dilution, as necessary, to avoid any primary irritating properties.

LEUKOPENIC INDEX IN ALLERGY

To the Editor:—I have only recently read Dr. L. P. Gay's article about the leukopenic index in The Journal of March 21, 1936. Please inform me if subsequent events have shown the leukopenic index method to have as much practical value as was hoped for. If so, is there any later helpful article available on the subject that gives further information on the method? R. D. Holt Jr., M.D., Meridian, Texas.

ANSWER.—The technic, pitfalls and value of the "leukopenic index" in allergy are adequately discussed by the late Dr. Warren T. Vaughan in his book "Practice of Allergy," St. Louis, C. V. Mosby Company, 1939. Vaughan first suggested the leukopenic index as a method of study of food allergy. It is a modification of part of the liver function test suggested by Widal and his co-workers. In his discussion (chapter XXII, pp. 228-244) Vaughan gives the technic in minute detail, emphasizing the care required and the many possibilities for error. He also mentions, though briefly, those workers who found the leukopenic index unreliable and of no clinical value (Loveless et al., Brown et al., Hill et al.). His final sentence in this discussion, written in 1939, is as follows: "We must conclude that the leukopenic index is still in the experimental stage and cannot be discussed at this time as a routine diagnostic procedure in allergy." Most allergists would agree that this sentence today in 1944 is a fair summary of the degree of usefulness of the leukopenic index. Fewer allergists make use of it today than six years ago.